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THE OLD MOTOR SYSTEM AND THE NEW*

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Among the various noteworthy advances made by neurology since the beginning of this century none is more striking than that concerned with our knowledge of motor disease.

A single illustration will serve better than any long account to demonstrate this progress. In the third volume—devoted to diseases of the nervous system—of Sir William Allchin's "Manual of Medicine," published only twenty years ago and remarkably modern in its outlook, paralysis agitans finds a place under "Functional Diseases," between occupation neuroses and night terrors. Today, no student of the subject can pick up a neurologic journal, English or foreign, without a likely chance of finding therein contributions dealing with the phasic and static activities of the motor nervous system, with muscle tonus, extrapyramidal motor disease, postures, attitudes, and involuntary movements. Along with the advance of which these innumerable papers are the token, however, there has come increasing recognition of difficulties, or, rather, those who would seek to grasp the established truths are still conscious of a good deal of groping. The reasons for this state of affairs are seemingly manifold: (1) Many clinical cases are remarkable for the complexity of the motor phenomena encountered. This is particularly the case when disorders of tone and attitude are coupled both with paralysis and with involuntary movements. (2) It is difficult often to separate the actions of different mechanisms which may be simultaneously involved. (3) Over-schematization of syndromes and too hard and fast ascription of particular symptoms to particular anatomic systems have in reality hindered knowledge, instead of augmenting it. (4) Too facile an interpretation of the clinical phenomena of disease by reference to the results of experimental neurophysiology has also been a disadvantage. (5) Experimental results are themselves sometimes in conflict, as are, unfortunately, the pathologic findings in not a few cases presenting clinical resemblances or identities.

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While, therefore, the gloom in which many of the problems of the motor system have been shrouded is in process of being dispelled, the light is perhaps not yet sufficient for recognition of more than the salient features of some of the various mechanisms as they now appear to stand out. In the present communication I shall attempt a brief survey, considering the subject of the old and the new motor systems from a threefold point of view: (1) from that of comparative anatomy and comparative physiology; (2) from that of experimental physiology; (3) from the standpoint of the clinician and the neuropathologist. A succinct account of the present position of knowledge as it appears to me will give an opportunity of indicating in what respects caution and criticism are still clearly needed, and of outlining several personal views to which further clinical and experimental research is at present leading me.

COMPARATIVE ANATOMY AND PHYSIOLOGY

As an essential preliminary to the study of the clinical phenomena of motor disease we must consider the old and the new motor systems from the standpoint of comparative anatomy and physiology.

In the vertebrate series the familiar corticospinal (pyramidal) efferent motor system only appears when the pallium or cortical "mantle" develops above or anterior to the original motor centers, which for the moment may be alluded to as "lower motor centers." According to de Lange this development of what later becomes the corticospinal tract, uniting an incipient pallium to the spinal cord, is first encountered in the higher reptilia. In birds, however, such descending fibers are so few as to be negligible, and their pallium (largely a visual and olfactory pallium) has been shown to be electrically inexcitable; hence Ariëns Kappers' view that in these vertebrates the "old" motor centers act vicariously for the "new." Be this as it may, it is only when we reach the lower mammalia that a pallial motor ganglion and a projection system therefrom to the spinal cord become permanent anatomic features of the nervous system.

What are the original motor centers of prepallial days? By the term "subcortical or lower motor centers" are signified, loosely, ganglionic groups at lower levels which, from the histologic character of their nerve cells and from their possessing fiber systems of descending type, are presumed to be efferent or motor in function. (1) The fundamental motor unit in this respect is the lower motor neuron, from ventral horn nerve cell to end-organ in striated skeletal muscle. Regarded from the viewpoint of phylogeny, it is the original, and simplest, unit of motor activity. The oldest motor centers are the spinal centers. (For the purpose of this communication, we need not descend further in the scale of living creatures than to those in which

a central neuraxis can be recognized.) (2) Further, in the whole vertebrate series, the basal part of the telencephalon or forebrain forms a prominent organ, known as the corpus striatum, and more or less tacitly assumed to be the highest center of the old motor system, the old "upper motor center." Evidence goes to show that, for the lower animals (fishes, reptiles, birds), the corpus striatum represents the farthest central "motor" development hitherto attained. Divisible into a paleostriatum (the globus pallidus of the higher vertebrates), as obtains in fishes, and a neostriatum (the putamen-caudate of the higher members of the animal series), as found added to the former in reptiles and birds, this fundamentally significant organ may be regarded, in Elliott Smith's words, as that part of the original cerebral hemisphere whereby impressions of smell, and other sense impressions, may bring their influence to bear on the nervous mechanisms regulating movement. If this is so, it must be a ganglion of a somewhat different order from the central motor cortex. At the very outset, indeed, we are faced with the fact that the differences between the old and the new motor systems, phylogenetically considered, are more striking than the analogies.

(1) We cannot be sure that the functions of the corpus striatum in creatures with little or no motor pallium are comparable to those of the motor cortex of higher animals. On the contrary, we are struck by the fact that there are considerable histologic differences between the two, and that the former, at least in the higher animals, does not, when electrically stimulated, give rise to any recognizable skeletal movement. It is conceivable, no doubt, that when the level of the mammalia is reached, the corpus striatum has already changed in function from what it may be in the case of fishes, reptiles and birds. In any case, we do know that it is closely associated, in the most primitive type of forebrain, with olfactory and possibly gustatory impulses, and that part of it is in fact an olfactory "cortex" or archipallium. Otherwise expressed, part of it, in the history of the animal series, must be supposed to exercise receptive or sensory functions. We cannot, therefore, on the grounds of comparative anatomy and physiology, consider the corpus striatum and motor cortex comparable without a good deal of qualification.

(2) Again, the striatal projection system is not similar to that of the motor area of the cerebral cortex, which is anatomically unbroken in its extent to the spinal cord; on the contrary, that of the corpus striatum is peculiarly complicated. It consists of an original "basal forebrain bundle," a tractus striothalamicus and a tractus striosubthalamicus in one, linking the organ with still lower, caudal, motor ganglia via the optic thalamus. The original efferent pathway from the paleostriatum is broken in the latter ganglion. It is important to bear

this in mind since clinical attention to the sensory thalamic syndrome has led to a certain ignoring of the motor disorders connected with disease of the ganglion; moreover, stimulation in apes of the thalamus (particularly of its lateral and the ventral part of its median nuclei) gives progression or locomotion movements—again an important consideration. The paleostriatum, once more, is linked definitely by a tractus striomesencephalicus to the midbrain. Thus the corpus striatum has no direct spinal projection system as has the motor cortex, a fact which of itself suggests that the original functional relation of the old upper motor centers to the spinal cord cannot have been identical with that of the new upper motor centers to the same part of the neuraxis. Indeed, as has just been remarked, it is an instructive fact that movements are obtained experimentally with much greater ease and certainty from various points within the optic thalamus than from the corpus striatum. The direct connection of the former with the spinal cord, via the posterior longitudinal fasciculus or otherwise, is undoubtedly as close as, if not closer than, that of the latter. We may legitimately hesitate, therefore, to ascribe motor functions to the corpus striatum which can be compared with those even of the optic thalamus. As already pointed out, the corpus striatum possesses a series of descending paths to the spinal cord which are interrupted in the optic thalamus, the regio subthalamica and the mesencephalon. At each of these places are collections of cells from which the links to the spinal cord take origin. The complexity of this projection system as compared with the simplicity of the corticospinal projection system must be kept steadily in view. It is immaterial for our present purpose to specify more minutely the various efferent paths by anatomic names; it is sufficient if we recognize clearly that the striatal efferent system has connections with the ventral horns of the spinal cord only via thalamus, regio subthalamica, and mesencephalon.

The place of the corpus striatum, therefore, in the old motor system is still rather obscure. The "primitive somatic motor fasciculi" of the lower animals are apparently derived in part from the corpus striatum, in part from the optic thalamus, or are in contact with efferent systems from both these ganglia, and it is incorrect to imagine the former purely motor in function, the latter purely sensory. Were there a direct striospinal path to neural mechanisms regulating movement, the problem would be easier than it is. In the absence of this, we are not justified in assigning motor *innervation* to the corpus striatum, though we cannot probably be far wrong in assuming that the primitive somatic motor fasciculi are the homologs of the corticospinal tracts in man, and that these are influenced at their oral origins by impulses derived from the corpus striatum, either directly or via the optic thalamus.

(3) The relation of the neostriatum (putamen-caudate) to the paleostriatum (globus pallidus) is one of the difficult subsidiary questions in a thorny subject. In animals whose pallium is still poorly developed the relation of these two parts of the corpus striatum to each other is far from being clear, and with increase of pallial action in the vertebrate scale the problem certainly does not become easier of solution. It has been supposed that in some ways there is a parallel between the development of the corpus striatum as a whole and that of the pallium; the relation of the neostriatum to the paleostriatum has been thought analogous to that of the motor cortex to spinal motor centers. But the analogy is misleading: We cannot say in actual fact that the function of the palliospinal system usurps that of the striatal system, for, as we have seen, it is distinctly doubtful if the corpus striatum is a motor organ of the innervation type; hence we cannot by any motor cortex analogy suppose that the neostriatum abrogates or inhibits the function of the paleostriatum. I mention this now because we shall see later how a speculative theory of differentiation of function as between the neostriatum and the paleostriatum has been erected on inadequate pathologic evidence.

EXPERIMENTAL PHYSIOLOGY

As a second preliminary to our clinical approach we must ask ourselves whether any *experimental distinction* can be drawn between the old motor system and the new.

To take the latter first, all of us are doubtless familiar enough with the characteristic phenomena of electrical stimulation of the excitable cortical motor area in man; we know how the musculature of the opposite side of the body is represented from toe to trunk, from trunk to arm and finger, from neck to face and eye, forehead, etc., in the precentral gyrus from above downward. We mention, in passing, the well established fact of reciprocal innervation; we know, further, that another characteristic feature of cortical innervation is its phasic nature. Only so long as the stimulus is applied do the corresponding muscle or muscles contract; with its removal, contraction immediately ceases; there is no after-discharge. This is true, also, of stimulation along the course of the corticospinal tract. For example, when flexion of the arm is produced by electrical excitation of the appropriate fibers in the pyramidal tract at the level of the crus (in the decerebrate animal) this flexion, as Graham Brown says, "climbs" during the course of application of the stimulus, its maximum being almost always at the point of cessation of stimulation. Cessation is followed by a very sudden relaxation, so that the arm "flops" in an extremely characteristic way.

Artificial excitation of the old motor system, on the other hand, leads us at once into problems which are far indeed from being solved.

As regards the corpus striatum itself, it may be definitely stated that investigation of the whole organ with a stimulating needle has failed, in the ape, to elicit any evidence of the localization of motor centers there, comparable to the centers of the excitable motor cortex. This is true both of the paleostriatum and the neostriatum, and is of fundamental importance, in view of the fact, already mentioned, that movements can be obtained from certain parts of the thalamus. It may be legitimately inferred that the motor functions of the corpus striatum cannot belong to the order of innervation, and we may, therefore, ask ourselves whether the corpus striatum may not stand to the rest of the old motor system somewhat in the relation of the higher motor cortex to the motor cortex proper (rolandic). This point will be referred to subsequently.

It is otherwise with the optic thalamus and the mesencephalon. Allusion has already been made to the progression movements obtainable from the median and ventral nuclei of the former ganglion.

In respect to the mesencephalon, noteworthy motor reactions are obtainable in the decerebrate animal. We owe largely to the work of Graham Brown our knowledge of this part of the subject. Unipolar stimulation of the cross section of the midbrain obtained by decerebration at the level of the anterior colliculi (anterior corpora quadrigemina), at a point entirely dorsal to the corticospinal tract in the crus, constantly produces a definite, specific postural motor reaction on the part of the animal experimented on. The area from which this result is invariably obtained is dorsal in the tegmentum and includes the region of the red nucleus, the part of the superior cerebellar peduncle running to it (tractus cerebellotegmentalis) and the posterior longitudinal fasciculus. The attitude is as follows: The head is tilted back and also twisted so that the face looks to the side stimulated; the homolateral arm is flexed and the opposite one extended; the leg of the same side, on the contrary, is extended and the opposite one flexed (as a rule); the tail erects and is bent to the stimulated side. The back is usually slightly convex to the opposite side.

When stimulation has ceased, the posture may continue unchanged for many seconds, even minutes.

From the appropriate area on the opposite side the posture is obtained reversed. As Professor Graham Brown and I are at present engaged in further study of this question I need not allude in greater detail to the matter of mesencephalic experimentation. Suffice it to say that the motor activities evoked are essentially postural; they can be obtained by appropriate stimulation though the cerebellum is removed, but thereafter they gradually lose in duration. They can also be obtained, and

maintained for many seconds, or even minutes, in limbs all the posterior roots of which have been cut months before.

One of the important points for our purpose is to note how, in comparison with these postural activities, that of the corticospinal tract is fundamentally nonpostural, i. e., is phasic rather than static. It may be repeated that when stimulation of the corticospinal tract in the crus is stopped the contraction of the corresponding limb or limbs at once fails, and with great suddenness. Thus experimentation has shown conclusively that pyramidal motor reactions correspond strictly to the duration of stimulus, while extrapyramidal or nonpyramidal motor reactions do not.

Apart, however, from actual stimulation of mesencephalic foci, the phenomena of experimental decerebrate rigidity, as elaborated by Sherrington and others, can readily be obtained by transection at the level of the anterior colliculi. The animal experimented on assumes a bilateral posture of rigidity in extension, which in Sherrington's view is a close approximation to "reflex standing." All we need bear in mind at present is that when the corticospinal or new motor system is bilaterally and completely out of action, motor reactions, characterized by the adoption and temporary fixity of posture, come into being, or, rather, reveal their presence, the enduring existence of which is, under normal conditions, largely obscured by the changing phasic activities of the new system. To demonstrate them, the latter has as a rule to be *hors de concours*. In order that they may be thus revealed, mesencephalon, cerebellum, and spinal cord are left. While the cerebellum, as we have seen, doubtless plays its part, that part is not absolutely essential for the reactions. Further, the corpus striatum itself is out of action—a point to which attention is particularly directed. In the neuraxis as constituted by mesencephalon, pons, medulla, and cord, resides a postural motor activity which, if released by experimentation or by disease at higher levels, will show itself in phenomena of the kind that I have been describing.

In their recent valuable contribution to the question of decerebrate rigidity, Bazett and Penfield are led to the conclusion that the postural mechanism stimulated in the experiments I have outlined is not identical with that responsible for flexor or extensor (decerebrate) rigidity. They declare it impossible that the two should be identical. It may be pointed out, however, that the postures adopted in decerebration seem to be identical with those obtained by compounding the results of mesencephalic focal-point stimulation bilaterally, as far as head, trunk, and tail movements are concerned; if this is borne in mind, as well as the fact that the postural reactions obtainable from the mesencephalon are maintained, it may be for many seconds after the stimulus is removed,

then I think the resemblances are close enough to make it doubtful whether there are two entirely distinct mesencephalospinal *mechanisms* concerned with postural rigidity. I believe, however, that there are different components in one mechanism, which is not the same thing. This matter is referred to again immediately.

Unfortunately, we are not yet in a position to determine to what extent the phenomena of experimental decerebrate rigidity are due to release from corticospinal control, and how much to release from striatal control. We cannot for that matter at present be sure whether the action of the corpus striatum or of part of it—the neostriatum—is in reality one of control or inhibition of lower motor centers. The evidence furnished by disease, as we shall see, is suggestive, though not as yet conclusive. Further experimentation in this connection is being undertaken, in the hope that light will be thrown from that side on one of the most difficult aspects of the interrelation of the old and the new motor systems.

In his most recent paper Bielschowsky has assumed that in the rigidity of decerebration there is a component of striatal origin, in the sense that since striatal lesions are associated with rigidity, the removal of that organ in the process of decerebration should add an element of rigidity to that otherwise produced by the experimental lesion. This view is in my opinion open to objection, since the rigidity of decerebration is a specific extensor or flexor-extensor rigidity quite other than the generalized skeletal hypertonia of striatal disorder, as we shall see.

Taking, however, the neuraxis as "stripped" by experimentation, and extending from mesencephalon to cord, inclusive of the cerebellum, we cannot in the present state of knowledge assign the postural phenomena to a mechanism activated after one fashion only. There is a mesencephalic component, a cerebellar component, a labyrinthine component, and, indeed, a cutaneous component. Otherwise expressed, in decerebration the anatomophysiologic system concerned with posture is free to assert itself through stimuli from several different sources. In response to passive alterations of the position of the head in space, or relatively to the trunk, the decerebrate animal makes movements of the limbs and trunk which are presumably the result of influences reaching the spinal centers from the semicircular canals, via the pons, or from cutaneous end-organs in the neck, via the medulla (the "tonic-labyrinthine" and "tonic-neck" reflexes of Magnus and de Kleijn). We have seen that postural movements of the limbs can be readily evoked in the same animal at levels much above those of the vestibular system, viz., from the mesencephalon; while, if the cerebellum itself is not essential for them, we cannot ignore the fact that the connection of that organ with the mesencephalon is of the closest.

It is matter for great regret that the late Sir Victor Horsley never published the results of his cerebellar experimentation, conducted with his colleague Dr. Clarke. From personal communications, and from one or two brief allusions by others who also had the privilege of working with him (e. g., by Dr. Ernest Sachs) it is known that Sir Victor Horsley obtained movements of the head (resembling those from mesencephalic stimulation) by excitation of the corpus dentatum of the cerebellum. He told me that the movement was just like one of torticollis, and always occurred. Further, he was able in the same fashion to get the commencement of progression movements by excitation of the fibers of the superior cerebellar peduncle.

In a word, from or through thalamus, mesencephalon, cerebellum, pons and medulla, movements and attitudes can be mediated, but *not* from the corpus striatum. We have seen that they are postural rather than phasic activities. Even when they approximate to phasic action, as in stepping or progression movements, they never take place with the freedom and rapidity of corticospinal movements.

It cannot be too definitely urged that this assumption of attitude in rigidity takes place at the spinal cord level. When old and new systems, the former in its supraspinal portion, are both out of action, as in the "spinal animal" of the experimentalist, numerous motor spinal integrations are still possible—such as stepping movements, the "scratch reflex," the "extensor thrust," and so on. At the bidding of appropriate stimuli what remains of the spinal cord can carry out reflexes and automatisms which are sometimes of considerable complexity. The main feature of these experimental automatisms of the spinal animal is their invariability. For example, in the case of the scratch reflex of the spinal dog, Sherrington has shown that in response to a stimulus of 100 double induction shocks per second (practically a continuous stimulation) the reflex arc produces flexion at the hip about four times per second, and no increase of intensity of stimulus will overcome the refractory phase in virtue of which the response is as it is, or convert a rhythmic clonic beat into a maintained steady contraction. This fixity or organization of response is patently far removed from the "fluidity" of corticospinal innervation.

Our summary may be somewhat in the following terms: (1) We may conceive of the spinal cord as constituting the veritable oldest motor system, and as still capable, in complete isolation, of living and functioning, of exhibiting integrative combinations of movement in a more or less fixed and organized fashion. The patterns of these movements are as it were stamped on the cord from the earliest days in phylogenetic history; the tone they manifest depends on the intactness of the proprioceptive arcs for the various segmental levels of the cord. (2) These primitive spinal integrations can, however, be acti-

vated from a higher level, viz., that of the cerebellomesencephalopontile centers. When these, in their turn, are completely isolated from above, but remain in connection with the spinal neuraxis, then specific postures can readily be obtained, e. g., efforts at reflex standing; for the different segments of the body (head, trunk, limbs) postures are obtainable which are bilaterally symmetrical and which under suitable circumstances can be brought into action unilaterally. Various spinal units are "re-presented" (as Hughlings Jackson might have said) thus at this second level, in the sense that they can be combined from it; the ribbons guiding them can be handled by the centers situated above the cord but below the cortex and the basal ganglia. The tone of these (decerebrate) postures is to some extent, though not entirely, dependent on the integrity of the organ which represents in their totality, on the afferent side, the various proprioceptive arcs of the cord, viz., the cerebellum. Apparently from cerebellum, from mesencephalon, and from pons, these spinal units can be made to play, in various permutations and combinations, yet, once again, the types of response are more or less fixed and organized. (3) The crucial experiments of separation at a third level, viz., that which physiologically isolates the corpus striatum and the optic thalamus from the pallium, while they remain in connection with the levels below, are still largely wanting (Goltz's old experiments being in this respect unsatisfactory), and therefore discussion here at once becomes speculative. It is none the less probable that the spinal neuraxis can once more be played on from above, certainly from the optic thalamus, but not, apparently, from the corpus striatum. The fact that movement can be elicited experimentally from cerebellum, mesencephalon and optic thalamus, respectively—all via extrapyramidal paths—but not from the corpus striatum, might be taken to suggest that the relation of the latter organ to the others may be one of "superiority," possibly on the analogy of a "psychomotor" as opposed to a "motor" activity, as already suggested. I have shown (in collaboration with Walshe) how in certain circumstances failure to inhibit innervation is a feature of disease of some transcortical "psychomotor" paths, and it is at least conceivable that, in a different way, the corpus striatum, in a diseased state, may fail to "inhibit," or to "steady," the activities of motor mechanisms situated below it. Be this as it may, whatever component the corpus striatum adds to the innervations from the striatothalamic level, it seems to stand in a different position from all the others, and to be concerned more with tone control, with steadiness of innervation than with actual origination of it. (4) As for the influence of the cortex on all this complex potentiality of movement at mesencephalic and at spinal levels, we fortunately possess some experiments of Graham Brown which are in my opinion of the first importance and significance, and which appear not to have received the

attention they deserve. In the decerebrate ape Graham Brown produced the usual mesencephalic reactions already discussed, say postural flexion of the left upper extremity. While this was persisting, the appropriate crus (corticospinal tract) was stimulated. Immediate augmentation of flexion occurred; after withdrawal of this crus stimulus, one might expect the mesencephalic flexor after-discharge to remain unimpaired. But this is not the case. On the contrary, the postural after-discharge vanishes immediately, just as after an ordinary pyramidal stimulation. In other words, stimulation of the corticospinal system "wipes out" the existing postural reaction derived from stimulation of the non-pyramidal system. In Graham Brown's words, "non-postural cerebral activity seems to abolish postural midbrain activity."

The significance of this will at once be obvious to the reader. At any moment cortical, voluntary, activity obliterates that of lower motor centers; rapid, phasic changes are possible because of the master control of the cortex, the actual nature of the activity of which has now received physiologic demonstration.

CLINICO-ANATOMIC INVESTIGATION

Our approach from the clinical side should be without prepossession, and should give due weight to the findings of pathology. We should not allow ourselves to be unduly influenced by what we have learned from the foregoing brief sketch of some of the doctrines of comparative anatomy and some of the data of experimental physiology.

Still, we cannot be far wrong in holding to the double type of motor reaction in man—the phasic, modifiable, activities of the corticospinal system, and the automatic, postural, static, more organized and less modifiable, activities of the older motor system.

To begin with, then, it must be clear that in health both old and new motor systems are in action. The activity of one does not mutually exclude the activity of the other. If possibly some of the results of experiment appear to obscure this issue, let us be quite clear in the matter. If decerebration lays bare the functions of the old motor system as distinct from the other, it does not follow that in health there is not a fusion of the respective functions of the two. On the contrary, the obvious point has been emphasized by Strümpell that an indispensable preliminary to, and accompaniment of, conscious, volitional innervation is functional activity on the part of the static or postural mechanism. Normally, there is "neural balance" between the two. In the words of Mourgue, the apparatus for the autoregulation of attitude must be in being if cortical excitations are to effect voluntary movements and acts. Winkler expresses the same idea when he says that with each displacement of the head a given attitude of the whole body

is determined, and it follows that for each intended voluntary movement the body finds itself, reflexly or automatically, in such a position as to enable the appropriate contraction of the muscles to be attained at the moment of production of that voluntary movement. Simple as this may appear in theory, the mechanism for tonic autoregulation is none the less of considerable complexity, and its analysis in disease or, rather, the separation in diseased conditions of the activities of the different motor components is peculiarly difficult.

DISEASE OF THE CORTICOSPINAL SYSTEM

In an ordinary hemiplegia, familiar to every clinician, a destructive lesion of the pyramidal tract gives rise to a particular clinical picture. However diffuse, unspecific, unselective, the pathologic condition—for example, a hemorrhage implicating the internal capsule—as long as it is adequately inhibitory of corticospinal function the arm and the leg on the affected side assume a specific, selective "pattern." This simple fact is in itself surprising enough. The clinical result is the predilection-type, as it is sometimes called, of Wernicke-Mann—in the arm, adduction at shoulder, flexion at elbow, semipronation of forearm, flexion at wrist, flexion of fingers; by comparison, the "pattern" in the leg is one of relative extension, with some adduction at the hip, and with foot extended and inverted, and toes pointing down and in.

With unimportant variations and few (though none the less interesting) exceptions, this specific attitude of the contralateral limbs follows a diffuse interruption of the corticospinal or new motor system. It is impossible to get away from the fact that disease of that system releases an action-pattern innate in the spinal cord, a physiologic grouping, according to a specific scheme, of collections of lower motor neuron units. Into this pattern tone flows, also as a sequel to the lesion, so that the attitude is maintained and is only with great difficulty overcome or modified by forcible volitional innervation with what remains of the new motor system. A postural state has taken the place of a phasic state.

The meaning of this precise posture has given rise to a great deal of controversy, which cannot be entered on within the limits of this communication. I may for the moment allude to the view which sees in the hemiplegic attitude a regression to the climbing habits of our postulated animal ancestors, and refer the reader to the excellent criticism of this hypothesis by Mourgue. The careful investigations of Kraus and Rabiner, on the other hand, have resulted in the establishment of a formula for these patterns based on a consideration of the anatomic position (dorsal or ventral) of the muscles involved. They have shown that the formula for the extensor attitude of the leg—an antigravity posture—is *VDV*, i. e., ventral muscles are in con-

traction at the hip, dorsal at the knee, and ventral at the ankle. For the upper limb, however, the formula that corresponds is not found in hemiplegia, but in the extension-pronation posture which I have described as occurring in typical guise in decerebrate rigidity in man. Here for the arm it is also *VDV*, an antigravity attitude. Its "corresponding opposite," a flexion attitude, *DVD*, is not quite identical with the flexion attitude of the hemiplegic arm, since in the case of the latter the wrist is commonly flexed, as in the decerebrate posture, whereas in the exact opposite we should have extension.

The positions assumed involuntarily by the lower extremities in cases of paraplegia are similarly specific, however diffuse the lesions may be. We distinguish clinically a paraplegia in extension and a paraplegia in flexion. The former is common and familiar; the latter, less common, is as a rule encountered when increasing isolation of the lower section of the spinal cord takes place from spread of the lesion, amounting to a total transverse interruption of function. In addition, we note how in paraplegia involuntary movements of a spastic nature are prone to occur. We recognize involuntary flexor and involuntary extensor spasms, the legs drawing up spasmodically, or shooting out straight. Once more, we have occasional opportunity to observe how involuntary flexion of one leg is accompanied or succeeded by involuntary extension of the other. We know the various clinical procedures (e. g., that of Marie-Foix) employed to demonstrate these involuntary activities. Instead of describing them as defense reflexes, it conduces to clarity of conception if we regard them as more or less ineffectual attempts at reflex stepping or walking.

Briefly, in these released action-patterns resident in the spinal cord we see evidence of activity of the old motor system in proportion as the new is interrupted; they are not modifiable in the ordinary sense, but are on the contrary integrated according to fixed schemes. As already indicated, they are as a rule accompanied in action by an access of tonus, so that postures are maintained and involuntary movements are slow and spastic, with lingering after-discharge. Perhaps it is desirable to point out that a distinction should be and has been drawn between the "pattern" of an involuntary muscular action-group and the tonus accompanying its activity. Tone-producing mechanisms and pattern-producing mechanisms are not of necessity identical, however closely, as a rule, the two tend to synchronous action. Allusion will again be made to this point a little later.

I do not doubt that the isolated spinal cord is the seat of still other reflex motor integrations than those concerned with stepping. Disease brings out such integrations in respect to other physiologic groups. Especially in cases of total transverse lesion following gunshot wounds

of the cord have these been remarked. It is adding unnecessarily to the length of this paper to go into the matter more closely. I may, however, cite a case which has been under my care at the Star and Garter Home, a case of total transverse lesion of the cord. Cutaneous stimulation of the skin area including the external genitalia is always followed by tonic, lingering contraction of the toes in plantar flexion on both sides. The possible biologic significance of this and other reflexes that might be mentioned will doubtless suggest itself to the mind.

The question of the hypertonus accompanying these spinal phenomena is a study in itself. When the lesion is anatomically complete, tone depends on the integrity of the individual proprioceptive arcs of the segments that remain. It is quite impossible that any of the various other mechanisms associated with tonus control—labyrinthine, mesencephalic, cerebral, or cerebellar—should be here in action, since they are anatomically isolated.

DISEASE OF THE OLD (STRIATOSPINAL) MOTOR SYSTEM

Thanks to the labors of a number of neurologic workers belonging to different schools, English and foreign, the last decade has seen the introduction of order into a formerly very confused subject. The credit is due more to the well tried clinicopathologic method than to any other. As a consequence, we now know that certain diseases are with greater or less definiteness to be assigned to the corpus striatum and its projection system. For our present purpose I need only specify progressive lenticular degeneration, paralysis agitans, chorea chronica, and torsion spasm. A syndrome of the corpus striatum has been established by the Vogts, and independently and a little differently by myself, and still more recent work tends largely to confirm the outlines already sketched.

The cardinal clinical features of disease of the corpus striatum may be summed up in three words—variability in muscle tonus, the appearance of involuntary movements, and the absence of paralysis.

Muscle Tonus.—To take the matter of muscle tone first: In the great majority of cases of striatal (extrapyramidal) disease there is permanent increase of tone in the skeletal musculature; in a minority, the tone is variable from time to time, and may therefore be usefully described as constituting a condition of dystonia. A prominent characteristic of cases of progressive lenticular degeneration is the rigidity of the musculature generally, not merely of the limbs and trunk, but also of the face, throat, larynx, etc. It is of fundamental importance that we should remember that this hypertonicity seems to affect no particular groups, as flexors or extensors, but all groups more or less

equally. One of my patients, as he sat on the edge of his bed, slowly rolled over on to his side, a solid mass of rigid muscle, all the attitudes of trunk and limbs remaining fixed as he fell. When the forearm is passively flexed at the elbow, resistance is encountered in the extensors, and vice versa when the forearm is extended. Now we have seen that in corticospinal (pyramidal) disease there is a selective accession of tone, as in the flexed arm of hemiplegia, the extended or flexed leg in paraplegia. Here then, we have one means of differentiating pyramidal and extrapyramidal conditions.

Similar phenomena are highly characteristic of paralysis agitans and, more especially, of the remarkable number of postencephalitic parkinsonians encountered by the clinician during the last few years. Some of these cases are truly phenomenal in their generalized rigidity. I have my colleague Dr. Aldren Turner's kind permission to refer to a case under his care at the National Hospital. The patient, a man in the prime of life, lies in bed absolutely immobile, like a recumbent figure on a tomb, "soldered," as the French say, by universal rigidity, which extends not merely to trunk and limbs, but to the muscles of phonation, deglutition, even to the ocular muscles (though to a less extent). Handle him as you will, he moves *en bloc*. Yet with all this unbelievable hypertonicity his abdominal reflexes are present and a double flexor response is obtained.

Thus in paralysis agitans, postencephalitic parkinsonism, and kindred conditions there is, as it were, a flow of tonus into all groups indifferently, as opposed to the flexor or extensor tonus of corticospinal disease. I regard it as of great significance to note that no amount of bilateral corticospinal motor disease can produce hypertonus in all muscles indifferently; in double hemiplegia the tone-picture of postencephalitic parkinsonism is *not* obtained in its entirety by any means. It is true that in the latter condition there is a general attitude of moderate flexion, which means only that the flexor tonus rather predominates, yet there are other instances of the disease, certainly of idiopathic paralysis agitans, as is not well enough known, in which the back is much more erect, in fact slightly extended.

Of equal interest, if much less frequent, is the condition now usually called torsion spasm. In it, temporary hypertonus follows temporary hypotonus in a confused and irregular fashion; the limbs at one moment are contracted involuntarily in flexion, at another in extension, with varying tonic maintenance. As yet only two cases have been examined pathologically (Thomalla, Wimmer) and in each cirrhosis of the liver was found, coupled with changes in the corpus striatum, but also equally marked elsewhere throughout the brain, including the cerebellum, especially in the case recorded by Wimmer.

They do not therefore afford the same clearcut picture as do some other forms of striatal affection.

Involuntary Movements.—In respect to the involuntary movements of lesions of the old motor system, those that accompany striatal disease may be classified as belonging either to the group of tremors or of choreo-athetosis. Without doubt, and in spite of the assertions of some continental observers, tremor is much the more frequent of the two as far as the corpus striatum and its projection system are concerned. Only in a minority is choreo-athetosis met with.

It is essential that we should recognize the full import of the fact that the striatal lesions with which hypertonicity and involuntary movements are associated are destructive lesions. Whether there be a general disintegration and necrobiosis of the organ, bilaterally, as in progressive lenticular degeneration, or a more or less chronic outfall of cells and fiber systems, as in paralysis agitans, or an interruption of neuronic activity from a remarkable fiber overgrowth, as in the status marmoratus described by the Vogts, each and all are negative or destroying lesions, and it must follow that the mechanisms for the involuntary movements and the hypertonia or dystonia are nonstriatal. This conception has been familiar to the English neurologist since the days of Hughlings Jackson, but it has only recently received widespread recognition. In their recent communications, for example, the Vogts are compelled to admit that the hyperkineses resulting from disease of the corpus striatum are of "substriatal" origin. "Extrastriatal" or "nonstriatal" is preferable to "substriatal." They make no attempt, however, to specify or localize the mechanisms more particularly.

This clinicopathologic fact bears out, it will be seen, the views already adumbrated above, that the relation of the corpus striatum to the rest of the old motor system is one of tone control, and of steadiness of innervation. Remove its influence by disease, and cerebellomesencephalospinal motor mechanisms come into overaction in spite of the normal activity of the pyramidal system; tonic postures become overemphasized; in fact, a universal muscular rigidity appears, distinct from the selective rigidity of corticospinal disease; or, alternatively, incessant involuntary movements develop, over which the control of the master system, the corticospinal, is at best fleeting and imperfect.

I wish to draw special attention to the fact that the normal corticospinal system is unable to prevent the effects of striatal disease from making their appearance. Though we speak of it as the "last word" in motor control, it cannot inhibit the hypertonia and hyperkinesis of striatal disease. I believe we have here proof of the autonomous nature of the corpus striatum, which is to be expected from the fact that no corticifugal fibers enter it. The evidence I have adduced indicates how independent, in spite of its phylogenetic age, is its influence on the spinal motor centers.

Efforts have also been made by the Vogts to distinguish clinically lesions of the neostriatum from lesions of the paleostriatum, in an endeavor to bring the symptomatology of dystonia and hyperkinesis into a striatal scheme. They maintain that lesions of the putamen-caudate (neostriatum) are associated with involuntary movements (tremor, chorea, athetosis), and of the globus pallidus (paleostriatum) with rigidity. Bielschowsky, similarly, finds support for this view in his recent paper on the corpus striatum. Ingenious as is the scheme, it is open to objections, some of which can only be mentioned in passing. (1) Following Hughlings Jackson, I believe that tremor and rigidity are sometimes closely interrelated. Now in progressive lenticular degeneration, tremor and rigidity are both early symptoms, and the earliest lesion is without question in the putamen-caudate, the globus pallidus being intact. (2) Bielschowsky says that destruction of the globus pallidus produces a rigidity which masks the involuntary movements caused by implication of the putamen-caudate. Yet, in cases in which both parts of the corpus striatum have been destroyed, tremor may continue to form a very prominent symptom. (3) Tremor and choreo-athetosis are involuntary movements very different in type, and it is inconceivable that the same mechanism should produce both. (4) There is little satisfactory evidence of involvement of *specific* cell systems and fiber systems in the group of striatal diseases; it is impossible to have lesions of the putamen-caudate which do not, dynamically at least, implicate the globus pallidus; hence it is impracticable to attempt to dissociate their symptomatology. (5) Numerous cases are on record in which the lesions determining the appearance clinically of choreo-athetosis or of tremor have not been situated in any part of the corpus striatum. To speak, as the Vogts are compelled to do, of a syndrome of the corpus striatum of "thalamic origin," of "cerebellar origin," etc., is both confusing and unjustifiable.

We must, of course, accept the occasional occurrence of choreo-athetotic movements from lesions of the corpus striatum; they have been observed in a few cases of progressive lenticular degeneration and in cases of status marmoratus; nor in this respect must we forget the apparent association of hyperkineses of this kind with striatal lesions as in torsion spasm, or the seemingly definite lesions of the same ganglion in Huntington's chorea.

I have, however, repeatedly emphasized the importance of grasping the facts of the occurrence of choreo-athetosis and of tremor in lesions not situated in the corpus striatum; as regards the former, it has been definitely seen in lesions of the optic thalamus, regio subthalamica, superior cerebellar peduncle (Bindearmchorea), etc. I have elsewhere advanced arguments to show that the lesions allowing its occurrence are found mainly on the afferent cerebellomesencephalothalamocortical path.

Absence of normal corticipetal impulses allows the movements of choreo-athetosis to occur. It is essential that the corticospinal tracts should be, comparatively speaking, intact. If they are thrown out of action completely, by disease, the involuntary movements cease. It is of much significance to note that in decerebration such involuntary movements never occur. I have seen a case of infantile cerebral hemiplegia with athetosis and jacksonian epilepsy in which, during the twenty minutes of "exhaustion paralysis" after a severe fit, the athetosis always ceased in the affected limbs. This paralysis was of cortical origin. Clearly, were the impulses producing the athetoid movements reaching the spinal centers by some other route, the latter would still be open to their influence and the movements should continue. Horsley checked involuntary, persistent athetosis in an upper limb by excision of the corresponding motor cortex area. It is gratifying to find that the most recent experimental research, by Dr. Lafora of Madrid, confirms the views here once more outlined. He has produced persistent choreo-athetoid movements in cats by lesions of the cerebellar peduncle, mesencephalon, and regio subthalamica.

The problem of the association of *some* striatal lesions with the same clinical phenomena remains for solution. I suggested ten years ago that some intimate connection by striothalamic fibers, of which there are large numbers, might conceivably explain the facts. I have tried to show, in this paper, that the corpus striatum possesses quite peculiar motor activities, not those of ordinary motor innervation. The suggestion, as I figure it at present, is that the play of striatal impulses on the optic thalamus may resemble that of the cerebellomesencephalothalamic system, in the sense that both are afferent or thalamipetal, and that in circumstances not yet elucidated lesions on either path may occasion choreo-athetoid movement via the corticospinal system. No one who carefully studies the actual nature of choreiform movements can fail to be impressed with the fact of their resemblance to fragmentary volitional movement; they are subjectively purposeful and objectively purposeless; they appear to be initiated as though to perform some act, but they break off abruptly and are left "in the air." Movements of this sort cannot be obtained experimentally from the corpus striatum.

The case of tremor is somewhat different. Its association with midbrain and tegmental lesions generally is undoubted, and I have on previous occasions laid stress on the absence of any evidence to implicate the cortex in its production. Hughlings Jackson declared that "tremor differs from rigidity, not fundamentally, but in degree," and I have always maintained that herein lies the clue at least to *some* of its appearances. The mechanism of its production is linked to that for the production of (extrapyramidal) rigidity. Without here going further into this question also, I may say that I associate tremor with

the play both of striatal and of cerebellar impulses on the mesencephalon, and that in the case of the former tremor is more prone to be associated with exhibitions of rigidity than in the latter; indeed, with the latter the tonus of the muscles involved may be seemingly diminished. Besides, the tremor of paralysis agitans is clinically distinguishable from that, say, of disseminated sclerosis, and there must be definite differences in the exact mechanisms disease of which reveals itself in this particular variety of involuntary movement.

SIMULTANEOUS INVOLVEMENT OF CORTICOSPINAL AND STRIATAL MOTOR PROJECTION SYSTEMS

The compounding of lesions of the old and the new motor systems is the last matter I can possibly touch on at present. We have seen that in normal circumstances a constant interplay of old and new motor activities must occur. In diseased conditions in man we rarely get anything like complete outfall of function of one or the other system. Disease has, however, shown us that in lesions of the corticospinal paths, paralysis of voluntary movement is associated with the assumption of involuntary postures, produced by the release of function of spinal motor units, in action-patterns which must have some significance. Disease of the striospinal system, on the contrary, "allows" rigidity and hyperkinesis. The rigidity is much more universal than in corticospinal cases. The influx of tone is into flexor and extensor action-patterns more or less equally and simultaneously, with the clinical result already described.

Complete Interruption of Function.—In the condition which has been regarded as decerebrate rigidity in man, i. e., in that condition of complete interruption of function—both corticospinal and striospinal—produced by lesions of various kinds roughly speaking at the level of the mesencephalon, what do we find? Since the striatal system is out of action, we might expect the universal rigidity of the post-encephalitic parkinsonian, but this is not the case. We get an attitude or posture in extension which may fairly be regarded as indicative of an attempt at "reflex standing." As Kraus and Rabiner have shown, we have a specific formula for the innervation-pattern of arm and leg which is identical in the two. In other words, the posture produced by release of function when both old and new systems cease to act on the spinal neuraxis simultaneously is neither that of release from the one nor from the other.

Decerebrate attitude is a pattern-attitude, as is the case with corticospinal disease, but it is not that of single or of double hemiplegia or of, say, paralysis agitans. Into this innervation-pattern tone flows, but there is not that widespread, apparently nonspecific overflow that seems

to be characteristic of striospinal disease. The suggestion is, possibly, that the effect of release from cortical motor control outweighs the effect of release from striatal control.

We have seen that Graham Brown's experiments have demonstrated that cerebral activity abolishes midbrain activity; its control over the latter exceeds that of the corpus striatum, we may suppose, and when both systems are out of play the clinical result approximates rather to that which follows release from the former than to that consecutive to release from the latter. However this may be, we must agree there is a selective posture in rigidity, in the case of the double release, which is not so observable in the single (striatal) release; or, rather, we should say that the double release does not combine the two effects. The attitude of striatal release, say that of Parkinson's disease, may seem specific enough. We are compelled to admit that the effect of compounding the two release influences, if they are complete, is not quite what might be expected, and herein lies one more of the problems still calling for solution.

Incomplete Interruption of Function.—When the two systems, corticospinal and striospinal, are each incompletely out of action, we shall naturally find a complexity of symptoms which it is difficult to unravel. Take a case of infantile cerebral hemiplegia with athetosis, in which some voluntary movement of the affected limbs is still possible. Partial abrogation of corticospinal function causes the hemiplegic attitude to appear; this in its turn is constantly being modified by the appearance of involuntary movements, which for the sake of argument we may suppose of striatal origin. The result is a medley of paresis, hyperkinesis, and dystonia which we might almost despair of analyzing.

I am convinced, none the less, that by grasping the principles of corticospinal and of striospinal action, as I have tried to indicate them, by studying their effects in pure and uncomplicated cases exhibiting the results of disease of the one and of the other separately, we shall eventually reach a position from which we shall be able to solve the outstanding difficulties concerned with the human motor system in health and in disease. The clinician and the neuropathologist must contribute their quota to the attainment of this desirable end just as much as the experimental physiologist.

THE EXPERIMENTAL PRODUCTION OF BASAL GANGLION SYMPTOMATOLOGY IN MACACUS RHESUS *

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With the recent, rapidly progressing interest in the basal ganglions one finds the literature on the histology, pathology and function of these structures becoming remarkably extensive. Experimental evidence, however, to support the theories of the functions of the basal ganglions, is lacking.

In Wilson's [1] comprehensive review in *Brain,* 1914, he not only gives the results of his experimental work but outlines the literature from the year 1667 when Thomas Willis considered the corpora striata to be the seat of the sensorium. This review is so complete and well known that it would be but a repetition to give another historical sketch here. It is evident, however, that in his experiments he did not produce the symptomatology now attributed to lesions of the basal ganglions. Possibly this was due to confusion of the picture by gross lesions in the corticospinal tracts, or to the fact that the lesions were too circumscribed and apparently failed to involve enough cells to produce a clinical disturbance.

It was my aim to produce, experimentally, symptoms like those of paralysis agitans. Focal injuries having failed to do this, it was thought that more diffuse lesions might be produced by special poisons administered to monkeys. This method would have the advantage of causing a gradual injury to the tissues; lesions in various stages of development could be studied, and it might produce more typical symptoms.

In attacking the problem at this point the report by Edsall, Wilbur and Drinker [2] that workmen employed in an atmosphere containing manganese dust frequently develop symptoms similar in many respects to those of the parkinsonian syndrome, seemed to give such a hopeful lead that it was deemed worth while to try manganese intoxication of

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1. Wilson, S. A. K.: An Experimental Research into the Anatomy and Physiology of the Corpus Striatum, Brain **36**:427, 1914.

2. Edsall, D. L.; Wilbur, F. P., and Drinker, C. K.: The Occurrence, Course and Prevention of Chronic Manganese Poisoning, J. Indust. Hyg. **1**:183, 1919.

monkeys. Consequently over a period of eighteen months manganese chlorid was administered to four monkeys at the Long Island Hospital, Boston.

METHOD OF INVESTIGATION

Six normal monkeys of the *Macasus rhesus* species were chosen. These monkeys had recently arrived from India and were kept under close observation for three months before commencing the experiments, in order to acclimate and accustom them to captivity and to a carefully prepared and balanced diet. The diet consisted of water, boiled rice, fresh carrots, boiled and baked potatoes, wheat bread, turnips, roasted peanuts, cracked corn, oats and bananas. Throughout the periods of observation and experimentation the monkeys developed no pulmonary or gastro-intestinal disturbances.

Beginning with the fourth month and extending over a period of eighteen months, gradually increasing doses of a sterilized solution containing one milligram of manganese chlorid to 1 c.c. of distilled water was administered intraperitoneally with a 50 c.c. Luer syringe to four of these monkeys, the other two being kept as controls. Every other day injections were given, warm, but not hot, after sponging the site of the injection with alcohol. Care must be taken that the needle penetrates the abdominal wall into the peritoneal cavity and that all utensils and syringes with needles are sterile. After the injection a small amount of air is forced through the needle to clear it of the solution, as it was found by previous experiments on cats, that if any escapes into the muscles or subcutaneous tissues a large indurated area or even a slough may result. The only immediate effect of the injection is a slight indisposition on the part of the animal; he leans against the side of the cage for from ten to fifteen minutes after which he resumes his normal activities.

PROTOCOLS OF EXPERIMENTS

Monkey 1. Laboratory No. E. N. 1, 1921. (Control).—

Aug. 15, 1921.—The animal is normal and is put on regular diet. The animal remained normal and no injections were given.

May 7, 1923.—Eats well. No abnormal movements. No disturbance of posture or gait.

June 17, 1923.—This morning animal drags self about cage. Apparently sick but eats carrots. Hind legs are dragged but stands on them occasionally. Respiration not accelerated.

June 18, 1923.—No change.

June 19, 1923.—No change.

June 20, 1923.—A little brighter. Uses legs better but still droops a great deal. Is very quiet and does not resent stroking. Bowels normal.

June 22, 1923.—About the same.

June 23, 1923.—About the same.

June 24, 1923.—Found lying on left side with respiration rate of 56. Does not respond when handled. Caffeine 0.20 gm. was given subcutaneously but animal did not improve.

June 25, 1923.—Animal died during the morning. The necropsy revealed nothing abnormal in the head, thorax or abdomen.

Histologic Examination.—No abnormalities were found in the cortex, basal ganglions, cerebellum, pons, spinal cord, or peripheral nerves. The pituitary, lungs, heart, spleen, pancreas, liver, kidneys and muscles were normal.

Manganese Content of Tissues

	Mg. Per 100 Gm. of Tissue
Liver	0.120
Lung	0.055
Brain	0.032
Kidney	0.155
Pancreas	trace
Spleen	0.100
Heart	0.070

Monkey 2.—Laboratory No. E. N. 2, 1921. (Control).—

Aug. 15, 1921.—Animal normal., Put on regular diet. Animal remained normal. No injections.

May 7, 1923.—Eats normally. There are no abnormal movements nor is there any disturbance of posture or gait. No injections have been given.

June 19, 1923.—The animal is not eating well and appears to be quite sick. The limbs are used freely but animal droops markedly. The respiratory rate is not accelerated. The bowels are normal.

June 22, 1923.—The animal is apparently well again.

June 25, 1923.—The activities are normal.

July 1, 1923 to Sept. 15, 1923.—The animal eats well and all activities appear normal. No abnormal movements are noted.

Monkey 3.—Laboratory No. E. N. 3, 1921.—

Aug. 15, 1921.—Animal normal. Put on regular diet. No injections given.

Nov. 15, 1921.—5 mg. of manganese chlorid was injected intraperitoneally.

Nov. 16, 1921.—The animal shows no ill effects from the injection. No abnormal movements have been observed. The dose of 5 mg. of manganese chlorid was administered every other day until July 21, 1922, when the dose was increased to 10 mg. every other day. Up to this time the animal showed no abnormal movements.

July 23, 1922.—10 mg. of manganese chlorid was injected intraperitoneally. No abnormal movements observed.

July 25, 1922.—The injection of 10 mg. was repeated. The monkey does not sit on the perch or swing, and slight choreo-athetoid movements are occasionally observed.

July 27, 1922.—The injection was increased to 15 mg. of manganese chlorid. The movements are now quite definite and the monkey is becoming slightly rigid.

July 29, 1922.—15 mg. of manganese chlorid was injected. The choreic movements have almost disappeared and a fine tremor of the hands is observed. The dose of 15 mg. was repeated every other day until Aug. 16, 1922. During this period the movements had not changed in character.

Aug. 17, 1922.—15 mg. of manganese chlorid was injected at 11 a. m. The monkey continued to show fine tremors of the hands. At 7 p. m. the animal was found lying on its side apparently unconscious but breathing.

Aug. 18, 1922.—The animal is apparently dying, respirations very rapid and shallow. Died at 2 p. m.

Necropsy.—This was performed immediately after death. The brain and cord, in gross, appeared normal. The lungs only were examined and were reported "negative"! (This death and necropsy occurred during my absence and only the brain and part of the spinal cord were preserved.)

Histologic Report.—Spinal Cord: There is no cellular infiltration of the meninges and no perivascular infiltration. A normal number of cells is present in the white matter. The anterior horn cells appear normal, i. e., the cells are not swollen. The nuclei are central and the cells are not vacuolated (cresyl violet stain).

The meninges are normal, and the dorsal roots appear normal. There is no marginal gliosis and no evidence of neuroglia proliferation in any part of cord. Apparently there is a normal number of anterior horn cells present (phosphotungstic acid stain).

The dorsal and ventral roots, meninges, white and gray matter, and anterior horn cells appear normal. The blood vessels are normal and there is no perivascular exudate. No congestion of capillaries nor thrombosis is found (hematoxylin eosin stain).

Section of Medulla Oblongata and Portion of Cerebellum at the Level of the Olive: Occasionally a cell is observed in the medulla that seems to be slightly swollen, but these are rare. There is no definite cellular infiltration, but there appear to be a few more glia nuclei proportionately than one finds in the cord. The ependymal cells are normal, and a small section of the choroid is normal. As a whole the Purkinje cells appear normal (cresyl violet stain).

There is no neuroglia proliferation in the cerebellum although possibly there is a slight proliferation on the floor of the fourth ventricle. Otherwise the section is negative (phosphotungstic acid stain).

The cerebellum, medulla and meninges appear normal. No vascular changes are observed. There is no capillary congestion and the choroid is normal (hematoxylin eosin stain).

Section of Brain Through Hippocampus, Putamen, Pallidum, Internal Capsule and Thalamus: Very few ganglion cells are found in the putamen. Occasionally a large pallidal cell is found in this region. These are quite swollen, vacuolated, some of them showing chromatolysis, others being quite fragmented. The same picture appears in the pallidum. The cells of the thalamus and hippocampus are normal (cresyl violet stain).

There is no definite cellular infiltration, although the glia nuclei appear quite numerous. The blood vessels appear normal and there is no capillary congestion nor perivascular exudate (hematoxylin and eosin stain).

The neuroglia is quite dense in the putamen, and there is apparently an excessive amount in the region of the ansa lenticularis (phosphotungstic acid stain).

Manganese Content.—The brain contained 0.173 mg., the liver 4.906 mg. of manganese per 100 gm. of tissue.

Monkey 4.—Laboratory No. E. N. 4, 1921.—

Aug. 15, 1921.—Animal normal. Put on regular diet.

Nov. 15, 1921.—5 mg. of manganese chlorid was injected intraperitoneally.

Nov. 16, 1921.—The animal shows no ill effects from the injection. No abnormal movements have been observed.

Five milligrams of manganese chlorid was injected every other day until July 21, 1922, when the dose was increased to 10 mg. every other day. During this time the animal showed no abnormal movements.

July 27, 1922.—The animal appears to be normal. Dose increased to 15 mg. every other day.

This was continued until Nov. 15, 1922, when the dose was increased to 20 mg. of manganese chlorid, given every other day.

Nov. 19, 1922.—The monkey is beginning to show choreic movements; he does not sit on his perch, but prefers to sit on the floor of the cage.

Dec. 1, 1922.—The movements are now more of the choreo-athetoid type and the animal can remain on his perch only by grasping the side of the cage with both hands and both feet. The 20 mg. dose is continued every other day.

Dec. 30, 1922.—Condition practically the same as on Dec. 1, 1922. Same dose continued.

Jan. 17, 1923.—The movements are less noticeable, but the animal is becoming slightly rigid. Same dose continued.

Feb. 1, 1923.—The coarse movements have ceased and occasionally fine tremors can be seen in the fingers. The arms and legs are definitely rigid. Twenty milligram doses continued every other day.

March 2, 1923.—The fine tremors of the fingers are almost constantly present and the hands are contracting with the terminal phalanges of the fingers in extension. The monkey shows a gait which is very suggestive of propulsion.

This condition continued without change until April 19, 1923, when the monkey could not rise from his side nor take up food. The manganese injections were stopped, but the animal died on April 20, 1923.

Necropsy.—The brain, cord, trunk and abdominal organs, except the liver, showed no gross pathologic change. The liver presented large, very dark, reddish brown patches over its surface. These patches varied from 3 mm. to 2 cm. in diameter. On sectioning the liver the patches were found throughout the entire organ (Fig. 6).

Histologic Report.—Cortex.—As a whole the cortical ganglion cells appear quite normal, although the Nissl bodies do not stand out as sharply as they might. Eccentric nuclei are rarely found. The cells do not appear swollen. There is a questionable increase in glia nuclei. The ganglion cells are not disarranged. Occasionally one finds slightly vacuolated ganglion cells (cresyl violet stain).

The meninges appear normal and there is no edema of the pia. There is no evidence of perivascular infiltration or vessel change (hematoxylin-eosin stain).

There is no evidence of neuroglia proliferation in the gray or white matter. There is no marginal gliosis (phosphotungstic acid stain).

There is no evidence of myelin sheath degeneration (Van Heumann stain).

An occasional collection of fat droplets may be seen in the gray matter, but no fat droplets are found in the ganglion cells (Scharlach R. stain).

Section Through the Putamen, Pallidum and Internal Capsule: An average of about one half of the fibers running from the putamen to the pallidum show myelin sheath degeneration. The ansa lenticularis shows practically the same picture (Van Heumann stain).

Apparently there is a definite neuroglia proliferation in the region of the ansa lenticularis, which shows a breaking down in one or two areas. This area of destruction is quite dense, with neuroglia proliferation (phosphotungstic acid stain).

There is no evidence of any vessel change, nor of perivascular exudate (hematoxylin-eosin stain).

The cells of the putamen are narrow and shrunken. Some of the large pallidal cells appear large and swollen with eccentric nuclei and are scarce, some having extruded their nuclei (cresyl violet stain).

Section Through the Anterior Tip of the Caudate and Putamen Including a Small Section of the Cortex: Numerous bundles of fibers connecting the caudate and putamen have lost their myelin sheaths (Van Heumann stain).

The ependymal cells appear normal but are apparently pushed up by little hillocks of neuroglia about the caudate. There is no perivascular exudate. The blood vesels appear normal (hematoxylin-eosin stain).

There is a marked fibrillar proliferation under the ependyma beside the caudate. This appears more or less diffuse throughout the caudate (phosphotungstic acid stain).

The cells of the caudate are shrunken and pyknotic, and neuronophagia is present. Of the large pallidal cells some are shrunken and pyknotic, others are swollen and show chromatolysis, while others show marked neuronophagia. Many are vacuolated (cresyl violet stain).

Cerebellum: With the van Heumann stain and hematoxylin-eosin, the cerebellum appears normal. With cresyl violet the Purkinje cells appear normal, and with the phosphotungstic acid stain there is no evidence of neuroglia proliferation.

Pons: This region appears normal with the van Heumann stain.

The ganglion cells and nuclei appear normal as a whole, showing no chromatolysis. Occasionally one is found which is perhaps, slightly swollen (cresyl violet stain).

There is no evidence of hemorrhage or perivascular exudate; the meninges appear normal (hematoxylin-eosin stain).

The meninges and blood vessels appear normal. There is no evidence of neuroglia proliferation (phosphotungstic acid stain).

Muscle: The muscle fibers appear normal; there is no evidence of nuclear proliferation (eosin and methylene blue stain).

Lung: There is no evidence of pathologic change.

Spleen: This organ is normal.

Liver: There are numerous areas of necrosis accompanied by hemorrhages. The liver cells, to a great extent, are destroyed in these areas. Connective tissue proliferation is extensive in many of these areas (hematoxylin-eosin stain).

Manganese Content.—The brain contained 0.22 mg., the liver 5.58 mg. of manganese per 100 gm. of tissue.

Monkey 5.—Laboratory No. E. N. 5, 1921.—

Aug. 15, 1921.—The animal is normal. Put on regular diet. The animal remained normal. No injections were given.

Nov. 15, 1921.—Five milligrams of manganese chlorid was injected intraperitoneally.

Nov. 16, 1921.—The animal shows no ill effects from the injection. No abnormal movements have been observed.

Five milligrams of manganese chlorid was injected every other day until May 29, 1922.

May 29, 1922.—The animal is slightly rigid and shows a tendency to fall forward in walking. There are definite choreo-athetoid movements in the neck and arms. Ten milligrams of manganese chlorid injected.

May 31, 1922.—The condition of the animal is the same as on May 29, 1922. The 10 mg. dose was repeated.

June 2, 1922.—There is no change in the condition of the animal. The 10 mg. dose was repeated.

June 4, 1922.—The animal remains the same. The dose was increased to 15 mg.

June 6, 1922.—The choreo-athetoid movements in the neck and arms are becoming very pronounced. Fifteen milligram dose repeated.

June 8, 1922.—The animal remains the same. The 15 mg. dose was repeated.

June 10, 1922.—The monkey accidentally became entangled in a climbing rope and died of asphyxia.

Necropsy.—The brain appeared normal in the gross. The heart and lungs were normal. The abdominal organs were all normal excepting the liver. The liver both on the surface and on sectioning showed several irregular patches of a deep reddish brown discoloration. These patches varied from 3 to 10 or 15 mm. in diameter.

Histologic Examination.—Spinal Cord: The meninges appear normal and there is no definite cellular infiltration. The ganglion cells appear normal and stain well. There is no evidence of chromatolysis (cresyl violet stain).

The meninges appear normal. The ventral and dorsal roots appear normal. There is no evidence of any neuroglia proliferation either marginal or throughout the cord (phosphotungstic acid stain).

The meninges appear normal. The gray and white matter is normal. The anterior horn cells are normal. Here and there one observes a congested capillary but this change is not remarkable (hematoxylin-eosin stain).

Section of Pons: The meninges are normal and there is no evidence of neuroglia proliferation (phosphotungstic acid stain).

The ganglion cells appear normal (cresyl violet stain).

Nothing abnormal is noted. There are no vascular changes or changes in the supporting structures (hematoxylin-eosin stain).

Cerebellum: The sections are faintly stained, but the Purkinje cells appear normal (cresyl violet stain).

The meninges are normal and there is no evidence of neuroglia proliferation (phosphotungstic acid stain).

The sections are stained quite faintly. The Purkinje cells are normal. There is no evidence of neuroglia proliferation, nor perivascular exudate (hematoxylin-eosin stain).

Cortex: The ganglion cells appear to be normal (cresyl violet stain).

There is no evidence of neuroglia proliferation (phosphotungstic acid stain).

The section is quite normal and there are no remarkable vascular changes (hematoxylin-eosin stain).

Basal Ganglions: The large pallidal cells are swollen and many show vacuolization as well as neuronophagia. Many of the smaller type cells are also swollen. Only very rarely are any pyknotic cells found (cresyl violet stain).

There is no perivascular exudate and the vessels appear normal (hematoxylin-eosin stain).

There is an increase in neuroglia nuclei but no fibrillar gliosis appears (phosphotungstic acid stain).

There is no evidence of any myelin sheath degeneration (van Heumann stain).

Liver: There are extensive patches of necrosis present in which a large percentage of the liver cells has been destroyed. There are many red blood cells in these patches. Connective tissue proliferation is active and many young cells may be seen (hematoxylin-eosin stain).

Manganese Content.—The brain contains 0.51 mg., and the liver 8.88 mg. of manganese per 100 gm. of tissue.

Monkey 6.—Laboratory No. E. N. 6, 1921.—

Aug. 15, 1922.—The animal is normal. Put on regular diet. The animal remained normal and no injections were given until Dec. 15, 1922.

Dec. 15, 1922.—Ten milligrams of manganese chlorid was injected intraperitoneally. This dose was repeated every other day with no change in the monkey's condition up to March 22, 1923.

March 22, 1923.—The dose was increased to 20 mg. and given every other day.

April 3, 1923.—The monkey has difficulty in picking up pieces of cracked corn. Twenty milligram dose continued.

April 5, 1923.—There are quite definite movements of a choreo-athetoid type in the arms.

April 7, 1923.—The movements are now also noticeable in the neck.

April 9, 1923.—The movements are diminishing slightly. The animal continued about the same until May 7.

May 7, 1923.—There are marked choreo-athetoid movements of the neck, arms, body and legs.

May 9, 1923.—The movements continue. Dose increased to 25 mg. given every other day.

May 19, 1923.—Fair choreo-athetoid movements in arms, neck and legs. There is a marked tendency to fall forward in walking.

May 30, 1923.—Fair movements continue. The animal is still alive.

EXPERIMENTAL RESULTS

A study of the protocols shows that in a typical experiment the sequence of events is somewhat as follows: The monkey at first develops movements which are choreic or choreo-athetoid in type, later passing into a state of rigidity accompanied by disturbances of motility; then appear fine tremors of the hands and finally contracture of the hands with the terminal phalanges extended (Fig. 1).

The typical histologic findings in three of these animals have been as follows:

Brain.—The cortex shows a slight but evenly distributed chromatolysis with rare vacuolated nerve cells, no gliosis and no myelin degeneration. There are no meningeal or vascular abnormalities. Scharlach R stain showed no fat droplets in the neurons of the cortex.

In the putamen and caudate the cells are shrunken and pyknotic, many having lost their nuclei, and occasionally neuronophagia is observed. The large pallidal cells are few in number, swollen, vacuolated and show eccentric nuclei. There are scattered areas of gliosis which are occasionally quite dense (Fig. 2). Many of the fibers connecting the caudate and putamen have lost their myelin sheaths.

Fig. 1.—Typical paralysis agitans contracture of hands in Monkey 4.

Fig. 2.—Section through anterior portion of the caudate showing gliosis. Phosphotungstic acid stain.

In the globus pallidus some of the large pallidal cells are shrunken and pyknotic (Fig. 3), others are swollen and show chromatolysis, others have eccentric nuclei and vacuoles. In one case a definite loss of myelin sheaths was observed in the ansa lenticularis. There were areas of gliosis present in one case.

The cerebellum is essentially negative, although occasionally the Purkinje cells do not stain well. The pons as a whole appears normal, although occasionally a swollen ganglion cell is observed. There is no gliosis and the blood vessels appear normal. The spinal cord is normal

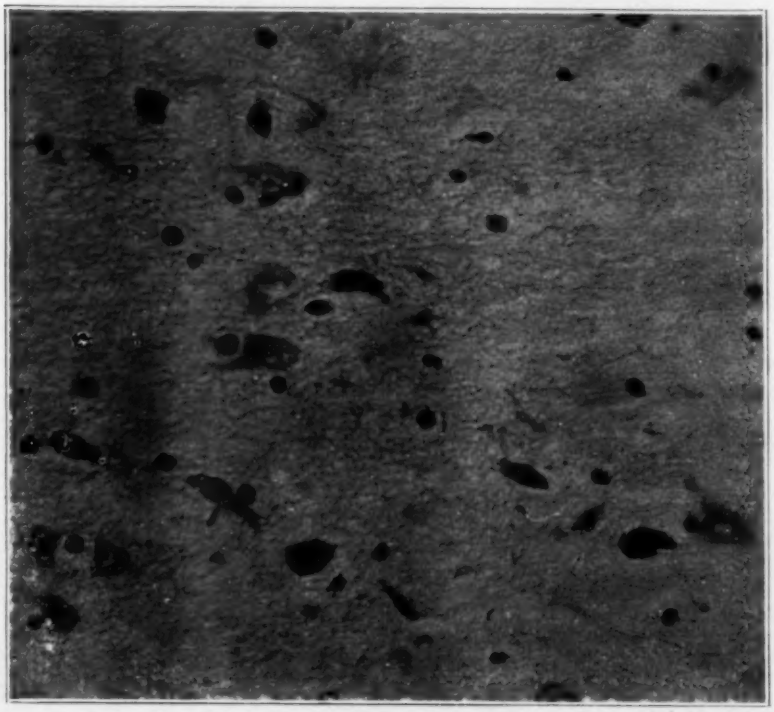

Fig. 3.—Section through pallidum showing shrunken and pyknotic cells with neuronophagia. Cresyl violet stain.

and the peripheral nerves show no Marchi degeneration. The muscle fibers appear normal and there is no evidence of nuclear proliferation. The lungs and spleen are normal.

The two livers show acute hepatitis, i. e., areas of necrosis (Fig. 4) with small hemorrhages and beginning fibrosis with scattered areas of chronic and more extensive fibrosis (Fig. 5).

The manganese content of the brain and trunk organs of all the injected animals was far above normal as is shown in the accompanying table. The brains contained about ten times the normal amount of

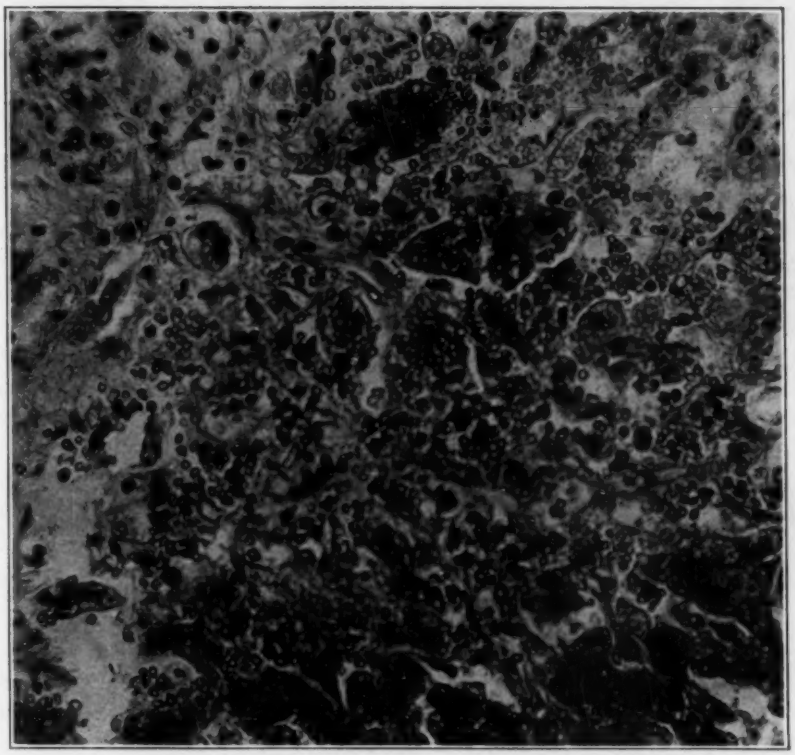

Fig. 4.—Liver showing area of acute hepatitis with hemorrhage. Eosin and methylene blue stain.

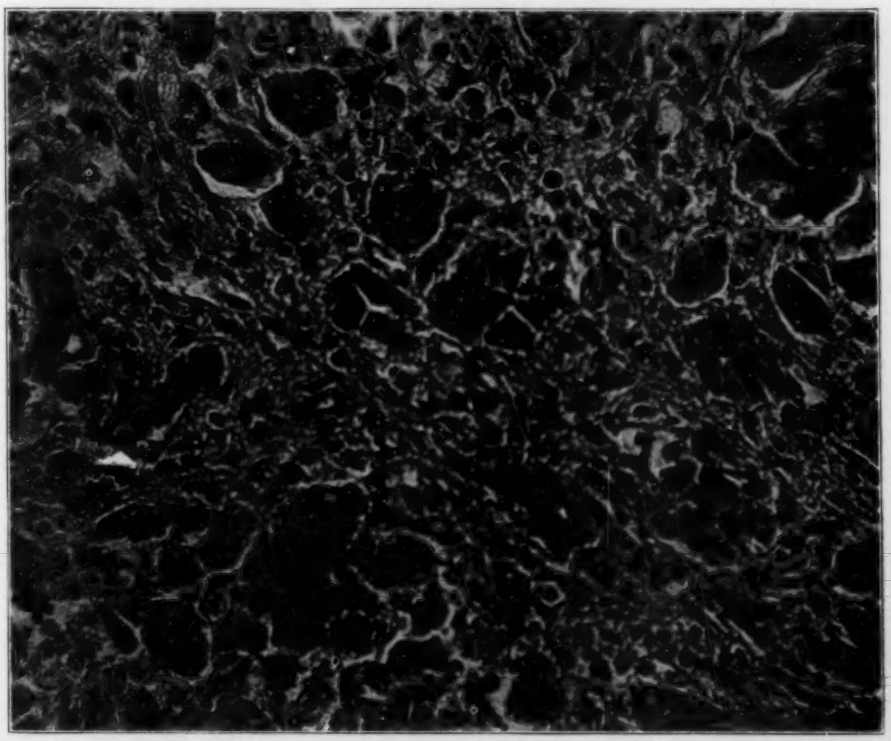

Fig. 5.—Area of fibrosis in liver. Eosin and methylene blue stain.

manganese and the livers about fifteen times. I am indebted to Miss Annie S. Minot of the Department of Applied Physiology of the Harvard Medical School by whom the manganese determinations were made.

Manganese Content Per 100 Gm. of Tissue of Monkeys That Have Come to Necropsy and Normal Figures for Comparison *

	Experimental Monkey		Normal Monkey		Normal Average for Cat, Dog and Rabbit		Normal Average for Man	
Animal Number	Brain	Liver	Brain	Liver	Brain	Liver	Brain	Liver
Monkey 1 (control)	.....	.....	0.032	0.120	0.047	0.2523	0.028	0.170
Monkey 3	0.173	4.906	0.032	0.120	0.047	0.2523	0.028	0.170
Monkey 4	0.22	5.58	0.032	0.120	0.047	0.2523	0.028	0.170
Monkey 5	0.51	8.88	0.032	0.120	0.047	0.2523	0.028	0.170

* Averages for normal tissues were taken from Reiman and Minot, Journal of Biological Chemistry 42: 329 (June) 1920.

COMMENT

I have already mentioned that Edsall, Wilbur and Drinker,[2] in examining a number of men employed in an atmosphere containing manganese dust, found that they frequently develop symptoms in many respects similar to the parkinsonian syndrome, but they also speak of the many points of similarity between their cases and Wilson's disease, progressive lenticular degeneration.

As one observes these animals passing into the stage of chronic poisoning, the rigidity and disturbance of motility, i. e., tendency to propulsion with choreo-athetoid movements, and later contractures of the fingers, it is striking how the symptoms simulate those of human cases now considered to be due to disturbances of the basal ganglions. Another striking fact, and one which is probably of great importance, is that we find pathologic changes in the liver (Fig. 6), but no abnormality in any other structure excepting the brain. As this work is but beginning I cannot say whether the liver changes precede the basal ganglion changes or vice versa. The relation between the liver and basal ganglion changes in Wilson's disease has not been worked out; possibly this method of experimentation will be a means of approaching that problem, as in these monkeys are found the dual lesions, namely, degenerative processes in the liver and basal ganglions.

The "shrinkage of the caudate" with gliosis, and marked degeneration of the lenticular fibers that run to the subthalamic nuclei and the red nucleus as described by Jelgersma[3] in Huntington's chorea, and

3. Jelgersma: Die anatomischen Aenderungen bei Paralysis Agitans und chronischer Chorea. Verhandl. d. Gesellsch. Deutsch. Naturforsch. u. Aerzte zu Köln, Leipzig, 1909.

the cell changes of the basal ganglions in paralysis agaitans described by Ramsay Hunt,[4] Bielschowsky[5] and C. and O. Vogt,[6] are all to be seen in the brains of these animals to a greater or less extent. The value in this, I believe, is that the brains of the experimental animals may be studied at any selected stage of the clinical picture, whereas with human material one must usually wait until senile changes or some intercurrent fatal disease confuses the histologic picture, and thereby greatly diminishes the ultimate value of the study. The chief difficulty here arises that no method has yet been found whereby the tolerance of the monkey for the manganese can be determined, so that premature deaths may be avoided; but by administering smaller doses over a greater length of time this difficulty may be solved. The analyses shown in the accompanying table are not yet sufficiently numerous to justify any conclusions, but it is interesting to note that the liver is the organ

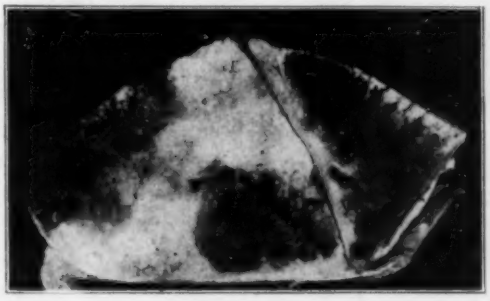

Fig. 6.—Section of liver in Kaiserling solution, showing patches of liver necrosis. From Monkey 4.

that is most heavily laden with manganese and that shows the most conspicuous pathologic changes.

CONCLUSIONS

From a study of these preliminary experiments it appears that in monkeys poisoned with manganese there were observed certain abnormal movements and disturbances of locomotion, which are usually attributed to lesions in the basal ganglions. The histopathologic picture in these animals shows definite changes, most pronounced in the striatum, pallidum and liver.

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4. Hunt, J. R.: The Efferent Pallidal System of the Corpus Striatum, A Consideration of Its Functions and Symptomatology, J. Nerv. & Ment. Dis. **46**:211, 1917.

5. Bielschowsky, Max: Weitere Bemerkungen zur normalen und pathologischen Histologie des Striärensystems, J. f. Psychiat. u. Neurol. **27**:233, 1922.

6. Vogt, C., and O.: Zur Lehre von den Erkrankungen des Striärensystems, J. f. Psychiat. u. Neurol. **25**:633, 1920.

A THEORY OF THE MECHANISM UNDERLYING INHIBITION IN THE CENTRAL NERVOUS SYSTEM*

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EXCITATION AND INHIBITION IN THE NERVOUS SYSTEM

In the various manifestations of the nervous system there are evidences of two distinct and mutually antagonistic processes, called *excitation* and *inhibition*. This dual function is represented in both the vegetative and cerebrospinal systems. It is evident in the lowest automatic activities of glands and viscera, as well as in the highest manifestations of the psychic sphere. And it may be stated as a general law that all neural function, irrespective of character or origin, is susceptible of increase or excitation and of decrease or inhibition.

In the vegetative nervous system, which represents the lowest functional level of the neural mechanism, the researches of Gaskell [1] and Langley [2] have demonstrated the presence of both excitatory and inhibitory nerves. According to Gaskell, inhibitory nerves are separate from motor or excitor nerves, and the process of inhibition differs essentially in its nature from that of excitation. Gaskell reached the conclusion that inhibitory function is constructive in character. In favor of this hypothesis he cites experimental observations which show that the increased action of the heart observed after vagus stimulation is of a different character from that occurring directly on stimulation of the accelerator filaments in the cervical sympathetic nerve. The effect of the latter resembles the usual action of a motor nerve and tends to exhaust the heart muscle, while the increased action observed after vagus stimulation is not of this character, but indicates that the sympathetic nerve now finds material on which to act, which before the vagus stimulation was wanting. In this sense the process of inhibition is not destructive or even merely neutral, but is definitely reconstructive in nature.

The researches of Von Uexküll [3] on invertebrates also show clearly the existence of both inhibitory and excitatory nerves, confirming the earlier studies of Richet and Biedermann. Von Uexküll states that

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* Preliminary report read at the Forty-Ninth Annual Meeting of the American Neurological Association, Boston, June, 1923.

1. Gaskell, W. H.: Inhibitory Nerves in the Involuntary Nervous System, New York, Longmans, Greene & Co., 1916, p. 68.
2. Langley: The Autonomic Nervous System, Brain **26**:1, 1903.
3. Von Uexküll: Die Härte der Muskeln, Ztschr. f. Biol. **56**:139, 1911.

formerly in the study of muscle function one had only to consider the phenomena of excitation, contraction and tonus. At the present time, however, the conception of fixation or "sperrung" of the muscle fiber has extended this point of view. Now one must recognize not only excitation and contraction, but also excitation and fixation as separate functions of the muscle fiber. He believes that there is a reciprocal innervation existing between these two functions, and that excitation of the one is associated with inhibition of the other; a conception which implies the existence of separate excitatory and inhibitory nerves.

There is also abundant evidence showing the existence of separate excitatory and inhibitory nerves in the vasomotor system and in the glands and viscera (Gaskell [4]). Indeed, in the whole realm of the vegetative nervous system the existence of separate neurons subserving the antagonistic functions of excitation and inhibition seems to be fairly well established.

In the central nervous system, on the other hand, the question of inhibition is much more obscure, and while we recognize the existence of an inhibitory function at all levels, no definite system of cells or neurons has as yet been associated with this function. Nor does there seem to be any general recognition of the necessity for separate inhibitory nerves such as exists in the autonomic nervous system.

Notwithstanding our inability to associate a definite neural mechanism with this function, a number of theories have been offered in explanation of the phenomena of central inhibition. One of these is the so-called drainage or diversion theory, which has been advocated by William James [5] and MacDougal.[6] Here inhibition is supposed to follow from drainage or diversion of nerve currents into other channels. Another theory which is much in favor at the present time is the synapse theory of Sherrington,[7] in which inhibition is supposed to result from blocking of the nerve impulse at the synaptic membrane of the cell. One of the oldest theories advanced by Wolkmann [8] was taken from the realm of physics. Here inhibition is regarded in the light of physical interference, the waves of nervous action reacting as do the waves of light and sound. Lucas [9] has recently utilized this theory in an attempt to explain the phenomena of central inhibition, based on the

4. Gaskell, W. H.: Inhibitory Nerves to the Vascular System in the Involuntary Nervous System, New York, Longmans, Greene & Co., p. 79.

5. James, William: Principles of Psychology, New Haven, Yale University Press **2**:584.

6. MacDougal: The Nature of Inhibitory Processes Within the Nervous System, Brain **26**:153, 1903.

7. Sherrington: The Integrative Action of the Nervous System, 1906, p. 101.

8. Wolkmann, A. W., cited by MacDougal, Brain **26**:158, 1903.

9. Lucas, Keith: The Conduction of the Nervous Impulse, "Central Inhibition," p. 82.

timing of the nerve impulse. Another important group of theories is founded on the intrinsic nutritive changes and the anabolic and catabolic activities of cells (Hering [10] and Gaskell [11]). Vernon [12] has also used this conception of inhibition in his "Biogen" theory of cell function.

It is a rather curious fact that in spite of the wide range which has been covered by these various theories, none indicates the possibility of there being two distinct types of cells subserving respectively the functions of excitation and inhibition, a relationship which appears to be so clearly established in the vegetative nervous system.

The present study is the formulation of a theory of central inhibition based on the existence of specific inhibitory cells within the central nervous system of man. Evidence will be presented in favor of associating this neural mechanism with the small nerve cells of Golgi (Type II) which form a cellular component of practically all ganglionic structures of the brain and spinal cord.

I have already referred to the existence of both excitatory and inhibitory neurons in the vegetative nervous system. In this system, when we speak of excitation or of inhibition it is associated with the idea of separate neural mechanisms as in the case of the heart, in which inhibition is related to the vagus, and acceleration of cardiac function is associated with the sympathetic nerve.

In the central nervous system, however, while we recognize the dual functions of excitation and inhibition, we are forced to use such general terms as cerebral inhibition or the inhibitory control of higher centers, which while implying the existence of an inhibitory function, gives no indication of its nature or cellular localization.

For example, the higher motor centers of the cortex are said to inhibit the activities of the lower motor centers of the spinal cord through the medium of the pyramidal tracts, and yet at the same time these tracts convey excitatory impulses to the motor centers of the spinal cord. If this be true, the pyramidal tracts (neokinetic system) are both excitatory and inhibitory in their relation to the spinal mechanism and do not reveal that duality of structure which has been shown to subserve these distinctive functions in the vegetative mechanism.

It is in an attempt to explain this peculiar discrepancy in our knowledge of the central nervous system that the present study is offered. What we know of the nature of inhibition and its underlying mechanism is so vague and so shrouded in mystery that any evidence bearing on this question, especially of a clinical and pathologic nature,

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10. Hering: Theory of the Functions of Living Matter, Brain **20**:245, 1897.

11. Gaskell: The Inhibitory Actions and Inhibitory Nerves, Tr. Eighth Internat. Med. Congress, Copenhagen **1**: Phys. Sec. 24, 1884.

12. Verworn: Zur Physiologie der nervosen Hemmungserscheinung, Arch. f. Anat. & Physiol., Abth. Sup., 1900, p. 105.

is of interest. It is in this spirit that the *specific cell theory* of inhibition is presented, with a full realization of the slender group of facts on which it is based and the gaps in our knowledge that are yet to be filled.

RELATION OF GOLGI CELLS TYPE II TO INHIBITION IN THE CORPUS STRIATUM

Anatomic Considerations.—The corpus striatum in man is divided by the anterior limb of the internal capsule into two parts, the nucleus lentiformis and the nucleus caudatus. The nucleus lentiformis has an external segment, the putamen, and an internal which is termed the globus pallidus. The putamen is identical in histologic structure with the caudate nucleus, and together they constitute the *neostriatum.*

The globus pallidus consists of two segments, an inner and an outer, a grouping which is produced by the fusion of nerve fibers in the lateral and mesial medullary laminae. This portion of the lenticular nucleus is older phylogenetically than the neostriatum, and is termed the *paleostriatum.*

Cell Types of the Corpus Striatum (Neostriatum and Paleostriatum).—From the standpoint of pathologic physiology, much greater importance is to be attached to the cellular types of this region than to the gross anatomic appearance and subdivisions.

The globus pallidus contains aggregations of pyramidal and large multipolar cells, which are histologically of the motor type. In addition to a characteristic arrangement of the Nissl granules, many of these cells contain a deposit of yellow pigment, and in other ways their appearance suggests the large pyramidal cells in the motor area of the cerebral cortex and the multipolar cells of the anterior horns of the spinal cord.

The caudate nucleus and putamen are composed of two types of cells of very different character— one small and the other large. The small cells are the more numerous and are of a stellate or polygonal form, and give the characteristic histologic picture to the neostriatum. These small ganglion cells have short axis cylinder processes and belong to Type II of Golgi's classification. They terminate in the outer or inner segments of the globus pallidus, and represent a short internuncial system which unites the caudate nucleus and putamen with the globus pallidus. Scattered among these smaller cells of the neostriatum are cells of larger size. These are large multipolar cells containing Nissl granules and often a deposit of yellow pigment. They resemble the large cells of the globus pallidus, and I regard them as subserving a similar function.

These larger ganglion cells of the pallidal type possess long axis cylinder processes and correspond to Type I of Golgi's classification.

They form an efferent projection system which unites the corpus striatum with important nuclei of the hypothalamic region.

Pathologic Considerations.—Some years ago, in pathological studies of the corpus striatum in paralysis agitans and Huntington's chorea, I found evidences of specific involvement of these two types of nerve cells (Hunt [13]). In juvenile and presenile paralysis agitans, the large motor cells of the corpus striatum were found atrophied and diminished in number, while the smaller ganglion cells were well preserved. This cellular atrophy (primary atrophy of the pallidal system) I regarded as the essential lesion of the disease. In Huntington's chorea, on the other hand, the small ganglion cells of the neostriatum were degenerated and greatly reduced in number, while the large motor cells which were affected in paralysis agitans were well preserved. This degeneration of the small cells of the neostriatum I regarded as the essential lesion underlying the symptom chorea.

Disease of the large motor cells of the corpus striatum therefore caused paralysis (decreased motion), while disease of the small neostriatal cells produced chorea (increased motion). One was a reduction of motion or a paralysis of excitation; the other was a release of motion or a paralysis of inhibition. In the corpus striatum there apparently existed two distinct types of cells with specific excitomotor and inhibitomotor functions. There is clinicopathologic evidence tending to show that inhibition in the corpus striatum is related to the small cell system, that is, the Golgi cells Type II. It therefore seemed reasonable to conclude that if cells of this type subserve an inhibitory function in the corpus striatum, it is not unlikely that cells of similar type exist elsewhere in the central nervous system, serving a similar function, and that central inhibition may be related to Golgi cells of this peculiar type (Type II).

Distribution and Character of the Golgi Cells, Type II.—Systematic writers on the histology of the central nervous system recognize three varieties of nerve cells, based on certain peculiarities of structure, which are described as unipolar, bipolar and multipolar types. The first two varieties are represented in peripheral structures. Unipolar cells, for example, are found in the spinal ganglia and the retina and those of bipolar configuration are present in the olfactory nerve, the retina and the ganglion spirale. The great cellular masses of the central nervous system, however, are composed of cells of the multipolar type.

13. Hunt, Ramsay: Progressive Atrophy of the Globus Pallidus. Contribution to the Functions of the Corpus Striatum, Brain **44**:490, 1921. Primary Atrophy of the Pallidal System of the Corpus Striatum, Arch. Int. Med. **22**:647 (Nov.) 1918.

Multipolar cells were still further divided into two great types by Golgi [14] in his classical histologic studies of the central nervous system. One variety is characterized by a long axis cylinder process which preserves its individuality and passes into a medullated nerve fiber. This corresponds to Golgi's Type I. The other variety is characterized by a short axis cylinder process which breaks up into numerous ramifications soon after leaving the cell, and represents Golgi's Type II.

The Type I cell is interfocal or interregional in its connections, passing from one nuclear structure to another. The great projection and association systems of the brain and spinal cord are composed of neurons of this type. In contrast to this, the cells of Golgi's Type II are intrafocal in distribution and do not leave the gray matter in which they take their origin. Many of the small nerve cells of the gray matter are of this type, and their axis cylinder ramifications contribute to the density of the fiber network of all ganglionic structures. Ganglion cells belonging to this type are found in all parts of the central nervous system; in the spinal cord, the brain stem, basal ganglia, the cerebellum and especially in the cerebral cortex. It is quite apparent as we ascend to the higher levels of the central nervous system which represents the higher degrees of differentiation and integration of neural function that these small cells show no tendency to diminish. Indeed they are especially conspicuous in certain layers of the cerebral cortex. So whatever their nature, they must be regarded as necessary adjuvants to the highest functions of the central nervous system. It is interesting to note that these cells are absent in the ganglia of the vegetative nervous system. This absence of the small cells of Golgi in the autonomic nervous system may have some bearing on my theory and their relation to inhibitory function. For, as we have seen, inhibition and excitation in the vegetative nervous system are subserved by separate neurons with long axis cylinders (Golgi's Type I).

Function of Golgi's Cells Type II.—At the present time little is known of the rôle which these small cells of Golgi play in the central nervous system. They are usually regarded as association cells. Golgi, in his original study, was inclined to associate the Type I cells with motor function and the smaller cells (Type II) with sensory function. The sensory theory was subsequently disproved and now finds few adherents.

Von Monakow and Cajal have both investigated this question and have attempted to find a rôle for these small cellular structures, which are so numerous in the central nervous system.

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14. Golgi, C.: Untersuchungen über der feineren Bau, des centralen und peripheren Nerven Systems, 1894, p. 81.

According to von Monakow,[15] they are to be regarded as association cells intercalated between sensory and motor neurons, which, according to him, are never in direct contact. These minute intercalary cells (Schaltzellen) are supposed to play a rôle in the association and redistribution of nerve impulses. The end arborizations of the long axis cylinders only terminate in relation to the body and dendrites of the Golgi's cell, Type II. The axon of the latter is then supposed to transmit the excitatory impulses to the motor cell.

Cajal,[16] who has made a special study of this type of nerve cell, accepts the association theory of von Monakow only in part. He denies that the function of these cells is merely to unite the sensorimotor pathways and states four reasons for his belief:

1. In the inferior vertebrates the unions of the sensory and motor pathways is affected directly, and not by the intermediary fibers of Golgi's cell (Type II).

2. The terminations of the afferent fibers are more voluminous than are the dendrites of Golgi's cell (Type II).

3. He knows of no region in which Golgi's cells (Type II) are alone in contact with one group of cells. On the contrary, Golgi's Type I and Golgi's Type II receive their excitation from a similar source.

4. The cells to which Golgi's Type II send their axons are always in direct communication with the sensory pathway.

Cajal, having disposed of von Monakow's theory, proposes one of his own which is even more fanciful. He suggests that these small cells function as accumulators of nervous energy, and serve as condensers in the central nervous system. He likens the Golgi cells (Type II) to a series of electrical condensers to which an afferent or efferent cord is attached. When, for example, an afferent fiber conveys an impulse to a Golgi cell, Type II, the cell itself immediately discharges, and this impulse is superadded to the original impulse of the axis cylinder; thus the neural tension is augmented. In presenting his suggestive theory, Cajal admits that there are no facts to substantiate this point of view.

Ariens Kappers,[17] in his studies of the cerebral cortex, refers occasionally to these small cells and more especially to the granular layer of

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15. Von Monakow: Gehirn Pathologie (Nothnagels spez) Path. u. Neurol. **1**:96, 1905.

16. Cajal: Rôle of Neurones with Short Axis Cylinders, Histologie der system nerveux de l'homme et du Vertebres **2**: pp. 150, 391, 590, 607 and 624, 1911.

17. Kappers, Ariens: The Phylogenesis of the Palaeo-Cortex and Archi-Cortex Compared with the Evolution of the Visual Neo-Cortex, Arch. Neurol. & Psychiat. **4**:161, 1909.

the cortex. He believes that they here subserve a receptive or sensory function and play a certain rôle in neurobiotaxis.

This, in brief, summarizes our present knowledge of the function of these small cells, which are so widespread in the central nervous system of man. It is quite evident that we have no certain knowledge of the function of this interesting type of cell, because there is no pathologic condition with which we are familiar which destroys these cells with a corresponding loss of function. It is for this reason that I attach a special importance to their degeneration in the corpus striatum with a loss of the inhibitory control of this mechanism and the production of chorea, for it is the only clinico-pathologic evidence which we have of the function of these cells based on a correlation of structural and functional loss.

RELATION OF A FUNDAMENTAL TYPE OF CELL STRUCTURE TO SPECIFIC CELL FUNCTION

In the previous pages I have given a brief sketch of what is known of the function of these small Golgi cells. The sensory, association and condenser theories do not rest on any secure anatomic or pathologic foundation. In the corpus striatum, however, the pathologic evidence shows that these cells subserve an inhibitory function, and as we have no definite knowledge of the function of these cells, I would generalize this observation and suggest the theory of an inhibitory function for this group of cells. I feel all the more justified in formulating such a theory as we have no recognized neural mechanism subserving the function of inhibition within the central nervous system, although the existence of such a system is rendered more than probable from its presence in the vegetative nervous system. It would be strange if nature were to discard absolutely a dual mechanism in the great central system which has been utilized throughout the sympathetic and parasympathetic systems.

Since cells of Golgi's Type II subserve an inhibitory function in the striatum, are we not justified in extending this hypothesis to cells of the same type in other portions of the nervous system? In other words, are there any grounds for assuming that there is a relation between a fundamental type of cell structure and specific cell function?

In 1910, Jacobson,[18] in a study of the relationship between structure and function in nerve cells, referred to Nissl's ability to detect the motor cells by a specific stain, and stated that he had attained similar results by another method. Jacobson was able by his method to determine the motor types of nerve cells with considerable accuracy, and he formulated

18. Jacobson, L.: Structur und Funktion der Nerven Zellen, Neurol. Central. **29**:1674, 1910.

the interesting hypothesis that identity of structure signified identity of function.

Malone [19] also carried out investigations along similar lines. He was able to show that the members of the somatic motor chain may be recognized by their histologic structure.

An important field of investigation was therefore opened to students of the central nervous system in the relationship of specific types of cells to specific functions.

Mention is made of these studies of Jacobson and Malone as showing the possible importance of a specific type of cell structure to specific cellular functions and the utilization of this histologic method in the determination of function of cells which are not accessible to the experimental method. It would also lend a certain support to my thesis that the identification of the Golgi cell Type II with the function of inhibition in the corpus striatum by analogy may be extended to the same type of cell in other portions of the central nervous system.

INHIBITOMOTOR CENTERS IN THE CENTRAL NERVOUS SYSTEM

In any hypothesis concerning the nature and mechanism of neural inhibition, the motor pathways have an especial interest because of our knowledge of their localization and the accessibility of these centers for experimental study.

Mention has already been made of the vegetative nervous system and the existence at this level of both excitatory and inhibitory fibers. And it is now generally accepted that the movements of involuntary muscle, including the heart muscle, which represent a transition from involuntary to voluntary muscle, are under the control of separate neural systems which excite or inhibit movement.

In the somatic musculature the situation is different. The peripheral nerves which convey impulses from the spinal cord to the skeletal muscles apparently contain no inhibitory fibers but only fibers of excitation, so that central inhibition, while it undoubtedly exists, is subserved by some mechanism more suited to the higher integrating and correlating activities of the central nervous system. Inhibition in the central nervous system is apparently effected by inhibition of the excitomotor center itself, this mechanism replacing the dual peripheral systems which serve these functions in the autonomic nervous system. Such an arrangement would simplify the mechanism of excitation and inhibition and lessen the complexity of the problem of integration in the central nervous system.

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19. Malone, E. F.: Recognition of the Somatic Motor Chain of Nerve Cells by Means of a Fundamental Type of Cell Structure, Anat. Rec. **7**:67, 1913.

In the theory of inhibition which I have proposed, this inhibitory mechanism is represented by specific inhibitory cells which in the present state of our knowledge must be classified as Golgi cells Type II. Cells of this type stand in close relationship to all of the excitomotor centers, so that afferent and efferent impulses passing to both inhibitomotor and excitomotor centers would produce the various manifestations of motility underlying the coordination of movement and posture.

Inhibition in the Motor Area of the Cortex.—In the rolandic area, which contains the excitomotor centers of the cerebral cortex and presides over the isolated-synergic movements of cortical origin (neokinetic system), there is, according to my conception, also an inhibitory cellular mechanism (neokolytic system [20]). This consists of numerous Golgi cells Type II which are represented in the cellular layers of the cerebral cortex, the fourth or granular layer being composed almost exclusively of cells of this type. At the present time, however, there is no pathologic evidence of the existence of such an inhibitomotor mechanism, although physiology and psychology both show clearly that an inhibitory mechanism must exist to carry on this function.

Inhibition in the Corpus Striatum.—In the corpus striatum which presides over automatic-associated types of movement (paleokinetic system), I have already indicated the relation of the small cells of Golgi to inhibitory function (paleokolytic system). Paralysis of the cells of this type in the neostriatum releases the striatum from control, and chorea results. This I regard in the light of a *striatal convulsive* manifestation, and in this sphere it is the functional analogue of cortical epilepsy or the spinal convulsion.

Inhibition in the Spinal Cord.—In the spinal cord, the essential excitomotor mechanism is represented by columns of the well-known multipolar cells of the anterior horns, the axons of which constitute the peripheral motor neurons. These cells, according to my theory, are inhibited by the small cells of Golgi which are present in the base of the posterior horns. This laterobasal group is composed almost exclusively of Golgi cells Type II, and the axons of these cells pass to the anterior horns, some crossing to the opposite side by way of the anterior commissure. This group of cells is particularly abundant in the cervical region and, according to von Monakow, the pyramidal tract fibers terminate in relation to these cells, which he assumes are association

20. I have used here the Greek equivalent for inhibition of—from *kolyo*, to prevent, to check, to hinder—the Greek root lending itself to the nomenclature which I advocated for the chief physiologic levels of the efferent system, namely, archeokinetic, paleokinetic and neokinetic (Hunt, J. R.: The Dual Nature of the Efferent Nervous System, Arch. Neurol. & Psychiat. **10**:37 [July] 1923).

cells, and relay the impulses to the motor cells of the anterior horn. According to my theory, these cells are specific inhibitory cells, representing an *archeokolytic* mechanism, the end arborizations of the pyramidal tract fibers passing to them as well as to the anterior horn cells. In such an interpretation the pyramidal tracts would convey impulses to both excitatory and inhibitory cells, both of which are necessary for the finer coordination of synergic movement. The experiments of Pick furnish additional evidence of the close relation of these small dorsal cells to the central motor pathways. He showed that strong stimulation of the motor cortex produced more marked changes in the small intercalary cells at the base of the posterior horn than were present in the motor cells of the anterior horns.

If the spinal cord contains columns of cells having a specific inhibitory function, pathology should furnish some evidence of the existence of such a mechanism. There is already ample proof of the existence of excitomotor centers in the anterior horns of the spinal cord; no such evidence exists for the specific inhibitory cells which I have postulated, although the convulsions of strychnin and of tetanus show clearly a loss of spinal inhibition.

The spinal convulsions following strychnin and tetanus are of special interest in their relation to inhibition. There is no evidence of motor or sensory loss, the only disorder being release of the spinal motor mechanism, in other words, a paralysis of inhibition. This I believe is due to a paralysis of the specific inhibitomotor center of the spinal cord, which releases the excitomotor mechanism with corresponding overaction to peripheral stimuli.

The researches of Baglioni [21] are of especial interest in relation to this question and would appear to favor my hypothesis. He found that it was possible to differentiate between the individual elements of the central substance of the cord by their reactions to certain poisons, strychnin and phenol having the common property of increasing the reflex excitability of the spinal cord to an enormous extent. The disturbances which are produced, however, are distinct. While strychnin poisoning causes tetanic spasms in all the muscles of the body so that coordinate movements are impossible, phenol poisoning does not abolish coordinated movements, but these are interrupted by rapid clonic contractions which produce constant attacks of tremor in different muscles.

Baglioni referred these fundamental differences to the different point of attack of the two poisons on the spinal cord. He found that if phenol were applied to the cells in the ventral part of the cord while the dorsal cells were spared, clonic contractions of the limbs appeared;

21. Baglioni: Cited by Luciani, Physiology of the Nervous System **3**:264, 1915.

but if strychnin was subsequently applied to the same region, it failed to elicit tetanic action. These and other experiments led Baglioni to conclude that the action of strychnin is confined to the cells of the dorsal part of the cord (which he termed the sensory or coordinating ganglion cells of the dorsal horn), while phenol has a selective action on the cells of the ventral part of the cord (motor ganglion cells of the ventral horn).

In subsequent researches on other animals, Baglioni confirmed and amplified the theory of the elective action of strychnin and phenol on specific central cells, and claimed that it is a physiologic method by which the existence of sensory central elements reacting to strychnin and of motor elements reacting to phenol can be readily detected.

These researches of Baglioni seem to indicate the existence of cells in the posterior columns of the cord subserving an inhibitory function, which are paralyzed by direct application of strychnin. These I would regard as specific inhibitory cells which are paralyzed by the direct action of the strychnin with the release of the spinal convulsions.

COMMENT

In the foregoing pages I have presented certain evidence which favors the theory of the existence of cells with specific inhibitory functions in the central nervous system.

While there is abundant evidence of the existence of inhibitory neurons in the vegetative nervous system, we have no proof at the present time of such a mechanism within the central nervous system. My studies of the corpus striatum would seem to throw some light on this important question. The function of inhibition in this organ is related to the small cells of the neostriatum which belong to Golgi's Type II.

These Golgi cells are found in practically all ganglionic structures of the central nervous system and must have an important function, as they apparently increase in number in the higher levels of the central mechanism.

They have been regarded as association cells, as condenser cells and as sensory cells, by different investigators. To these various views of their function I suggest another, namely, that they are inhibitory cells acting in conjunction with excitatory cells in the regulation of neural function.

Accordingly, I regard inhibition as we regard excitation as an active and specific manifestation of cell function, the two mechanisms working together in harmony as in the vegetative nervous system. This theory implies the existence of excitomotor centers subserving an

erethistic[22] function, as well as inhibitomotor centers subserving a *kolytic* function.

My theory of the underlying mechanism does not explain the nature of inhibition itself. Until more is known of excitation and the nature of the nerve impulse any such attempts to explain the nature of inhibition must be regarded as purely speculative. In this connection, it is interesting to recall the well-known researches of Gaskell on the innervation of heart muscle. He showed that the neural impulses of excitation and inhibition cause different electrical reactions. One is electronegative and the other electro-positive, which would appear to indicate certain inherent differences in these mutually antagonistic functions.

DISCUSSION

ON PAPERS BY DRS. WILSON, MELA AND HUNT

Dr. Charles K. Mills, Philadelphia: The stimulus to much of my own work in this direction, as well as some of my ideas, came from Dr. Wilson. My belief is that both a striatal and cortical region are concerned with the muscle tone, to which Dr. Wilson referred. Perhaps the cells of the putamen, to which Dr. Hunt has referred, are associator rather than association cells, and as I use the terms I believe there is a difference between them. I do not like the word "inhibition" as it is so frequently used. In a certain sense it may be correctly used; but what occurs with regard to the functions of both the striatum and its correlated cortex is an active innervation, or the release of one of these two great regions from active innervation.

My views (and they seem to be borne out to some extent by what has been said in two or three papers), are that the striatum, and especially the putamen of the striatum with its peculiar cellular system, is an associator organ for tone, and it associates the synergic movements which come from the cerebellar system, enabling them to be discharged *en masse*, instead of in isolated movements. The symptomatology of the striatum is, in the case of a destructive lesion, due to something elsewhere released. So far as motor manifestations are concerned, it is the differentiated movements of the cortical region which are released. It is for this reason that we get these curious involuntary and unrhythmized movements which are so frequent, and so well-known in striatal disease. It is the withdrawal of the associating innervation that leads to the result. Structurally, just how this association takes place may be a question. Of course, we well know there is no projection system between the cortex and the putamen. I am not so sure that it is entirely proved that there is no associating fiber system. The whole procedure may take place through the pallidum to the ruber and subthalamus, thence to the thalamus and from there to the sensory, motor and premotor cortex.

The independence, as well as the interdependence of the extrapyramidal and pyramidal systems should always be emphasized. For a considerable time, I have believed that the tonic tonectic or tonic innervating system is practically the same as the emotive system, the system concerned with emotional expression.

Dr. Frederick Tilney, New York: Under the leadership of Dr. Wilson, clinical, experimental and physiologic evidence is rapidly accumulating, bearing on the fact that the extrastriatal control over motion is perhaps secondary to

22. From the Greek verb, erethizo, to provoke, to excite.

another very important influence exerted by the mesencephalon. I feel great pleasure in being able to corroborate Dr. Wilson's idea by another method. It is certain that in the early development of the species which we have studied, very complex movements and performances may be carried on in the entire absence of any connection with the striatum or of any connection with the so-called new motor system.

It would seem, on the basis of myelogenetic study, that somewhere in the mesencephalon—it may be the substantia nigra, as we predicate, or in the inferior colliculus, which is probable from the fibering which I have seen there —the control of motion in the early stages of development is most important. Therefore, that part of the axis which lies caudal to the striatum plays an outstanding part in the control of the more simple automatic associated movements.

So far as I am able to say, a mammal, if thrown into the water on the first day after birth, will swim. This performance obviously has the object of keeping the head above water and the nostrils free, in order that respiration may be carried on. These complex automatic associated movements in swimimng may be carried on in the absence of any connection with the corpus striatum, for in the cat it is not until the twenty-eighth day, as shown by myelinization, that the real definite connections with the striatum are established. At that time the animal is able to carry on very much more complex movements, such as those of walking in the true mammalian fashion, jumping and running. Therefore, on the basis of our investigation, I subscribe to all that Dr. Wilson has said with reference to the old motor system and believe that the corpus striatum in itself is a very complicated part, belonging to the newer-old motor system, and even perhaps not very much older in point of time than the motor cortex itself.

Dr. S. A. Kinnier Wilson, in closing: I tried to point out the importance of mesencephalitic action in regard to the motor system, and to take away from the corpus striatum a certain amount of motor function that has been attributed to the motor system. The corpus striatum is motor and the optic is sensory. In reference to the question of negative lesions and positive changes in function, Hughlings Jackson used the expression, that as a result of disease, we had physiology and difficulties. If pathologic symptoms are explained by a part of the nervous system which remains, and not by the part which is diseased, better results will be obtained.

TUMOR IN THE REGION OF THE FORAMEN MAGNUM *

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The rareness of tumors in the region of or in the medulla oblongata, the indefinite symptomology which tumors in this region present and the character of the tumor found in the case to be cited, justify the following report.

REPORT OF CASE

Clinical History.—M. I., a woman, aged 40, with unimportant family history, except that a brother was mentally deficient, was referred by Dr. John B. Roberts. She had been in good health until six years before when a uterine fibroid was removed in which there was no evidence of malignant disease. Three and a quarter years ago she was knocked down by an automobile, her skull was fractured, and she remained in the hospital for one month. After this accident she complained of pain in the back of the neck which continued until death. She was, however, able to follow her occupation of stenographer and bookkeeper. The illness which terminated in her death was alleged to have begun a year previously and consisted of pain, stiffness and a feeling of rigidity in the back of the neck. She carried on, however, until two months before entering the hospital, when she was confined to bed. An examination by Dr. S. F. Gilpin revealed a slight weakness of the left arm and leg. Three weeks before admission to the hospital the weakness in the left arm rapidly progressed to total paralysis. This was ushered in by a feeling of numbness and tingling in the arm. Power in the leg was rapidly lost at the same time. The neck became rigid also and there was a tendency to turn the head to the right. The rigidity, however, was not great and could easily be overcome.

The patient was admitted to the polyclinic division of the Graduate School of Medicine of the University of Pennsylvania, Oct. 16, 1923, when, in addition to weakness of the left arm and leg, there was weakness of the right arm which in a few hours became total. A few hours later the right leg became totally paralyzed. The eye grounds had been examined by Dr. Edwin B. Miller, Aug. 14, 1923, with negative findings except that the ratio between the arteries and veins instead of being as in the normal 2:3, was 1:2. No study was made of the fields of vision. The Wassermann reaction was negative on Aug. 21, 1923. There had been some disturbances in speech for several weeks. She had spoken in a low tone of voice, but after admission to the hospital she was unable to speak, for the most part, above a whisper. A week before admission, she had some trouble in swallowing, which improved before admission, but later, on swallowing liquids, these regurgitated into the nose.

Examination.—When examined by me on Oct. 17, 1923, there was no paralysis of the facial or ocular muscles, or of the motor or sensory fifth nerves, and the tongue was protruded in the median line. There was relaxation of the palatal muscles on the right side, the uvula being drawn over some-

* Read before the Philadelphia Neurological Society, Nov. 23, 1923.

what to the left, and this became more apparent when efforts at phonation were made. There was absolutely no voluntary movement of either arm nor of the left leg, and the paralysis was of flaccid type. There was slight power in the right leg, but in a few hours this was entirely lost. The respirations were thoracic in type. The abdominal and plantar reflexes were absent. There was no Babinski sign, nor Oppenheim reflexes. The knee jerks were increased on both sides, but more on the right. The arm jerks were absent on the left and present on the right side. There was hypalgesia, irregular and widespread, over the entire right arm up to the level of the deltoid muscle with the exception of the palmar surface of the hand. On the left arm hypalgesia was present except on the palm and ulnar side of the forearm and extended to the level of the deltoid. The entire right leg was apparently hypalgesic. She could recognize a pin point all over the left leg. She was also hypalgesic on the right side of the trunk anteriorly and posteriorly as far up as the third thoracic spine. Further studies of sensation were not made at this time on account of the grave condition of the patient. There was some complaint of pain in the left popliteal space but none elsewhere. The respiratory murmur was faint, the respirations 20 per minute.

By the next day the loss of sensation had become practically complete in the limbs, trunk, and cervical region, and the entire trunk and limbs were totally paralyzed. There were no band sensations of the chest, waist, or legs. At no time was there double vision or implication of the eyesight.

Spinal puncture showed increased pressure. The cerebrospinal fluid contained 6 cells per cubic millimeter with positive globulin tests. The colloidal gold reaction was 0112321100. The patient died suddenly on the third day after admission to the hospital, of respiratory paralysis.

Necropsy Findings.—At the necropsy a tumor was found plugging the foramen magnum. It had pushed the medulla oblongata over to the right and posteriorly. The tumor rested over and completely covered the entire foramen magnum and was adherent to the dura on the left side only. It was easily dissected away from the dura. The tumor on the inferior surface measured 4.8 cm. x 4.5 cm. x 3 cm. Adherent to it and stretched over it were the ninth pair of nerves. None of the other cranial nerves was implicated.

Dr. Case made the following report of the examination of the specimen: "It looks not unlike the prostate gland in shape. The upper surface is convex and uneven due to rounded projections of varying size. In places the surface is distinctly granular. The under surface is slightly concave and is white while the rest of the tumor is distinctly red. The cut surface is light pink. In consistency the tumor is moderately soft but not friable. The specimen was fixed in Zenker's solution. Microscopically, the tumor is very cellular, supported by a fibrous stroma of dense adult connective tissue. The stroma is arranged in large trabeculae from which smaller strands extend in amongst the cells, dividing them into incomplete 'alveolar like' groups. In some of these groups there is a tendency toward a concentric arrangement. The cells vary in shape though they are elongated for the most part. The nuclei stain well. Between the cells and groups of cells there is, in places, interstitial edema." Diagnosis: Dural endothelioma.

COMMENT

The symptoms presented by this patient that stand out as important localizing symptoms are pain in the posterior cervical region with torticollis, paralysis of the muscles of the right side of the uvula and the

right side of the tongue, the rapidly progressing paralysis of the limbs, which, according to the history, began with slight weakness of the left arm and leg as long ago as August, 1923. The paralysis of the limbs, it must be noted, was rapidly progressive, dating from ten days before admission to the hospital. Feebleness of the voice, which was not constant, and slight difficulty in swallowing liquids, began shortly before admission to the hospital.

The pain of which the patient complained in the cervical region must have arisen from the stretching of the cervical roots, since this area is supplied by the second and third cervical roots. The paralysis of the uvula muscles and the right side of the tongue, the feebleness of the voice, and difficulty in swallowing, point to an involvement of the medulla oblongata. These symptoms did not stand out very clearly in the history and at the time she came under observation their importance was overshadowed by the rapidly increasing paralysis of the limbs. At this time the sphincters of the bladder and rectum were implicated and this together with the sensory changes, which extended below the level of the third thoracic spine and from a similar level on the arms, suggested a rapidly progressive myelitis.

The case is extraordinary and interesting as showing the absence of symptoms referable to the medulla oblongata until a short time before the fatal termination, with the exception of the pain in the neck and the torticollis.

Tumors of the medulla oblongata are comparatively rare, and are often symptomless, being discovered frequently for the first time at the necropsy table. A fairly exhaustive study of the literature fails to reveal a case exactly similar to the one reported. There are examples of intramedullary tumors of the medulla oblongata, such as the angiomas, cysticerci, fibromas, gliomas, gliosarcomas, and gummas.

Frazier and Spiller [1] have cited a case in which the tumor of the cervical region extended into the foramen magnum, and Cushing [2] includes in his collection of the meningiomas a case in which the tumor was situated anterior to the medulla oblongata, partially invading the foramen magnum. The last two cases are the only ones which resemble the one under discussion. Cases have been reported in which both the pons and the medulla oblongata have been involved. In 1865, Ladame [3] could find only nine cases in the literature of tumors of the medulla oblongata alone.

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1. Frazier, C. H., and Spiller, W. G.: Arch. Neurol. & Psychiat. **8**:455 (Nov.) 1922.

2. Cushing, Harvey: Brain **45**:282 (Oct.) 1922.

3. Ladame: Quoted by Erb in Ziemssens Handb. d. spez. Pathol. u. Therap., 1876, Vol. 11, Spez. Teil, p. 527.

The symptoms of tumor of the medulla oblongata in cases reported in the literature show considerable variation from what might be expected. Attention has been called to the presence of pain in the neck in a few cases. Though by no means constant symptoms, headaches, vomiting and vertigo occur fairly consistently. Paralysis of the facial and abducens nerves, with paralysis of the uvula, change in the voice from hoarseness to aphonia and alternating paralysis, i. e., paralysis of the face on one side, and hemiplegia on the opposite side, associated with ataxia, have been described, while sensory symptoms are less prominent. Choked disk has occurred. Dysphagia is not uncommon. The cases which show distinct features are not numerous.

In one case, a tuberculoma of the medulla, reported by Frey,[4] symptoms of pontocerebellar tumor were observed: choked disk, diplopia, dysphagia, facial palsy, bilateral trismus, positive Romberg sign, and reduced hearing, without sensory troubles or implication of the limbs.

In view of the fact that medulla oblongata tumors often present an indefinite history and symptomatology, more especially the extramedullary tumors, attention is especially called here to what seems to be rather a characteristic group of symptoms, namely, pain, stiffness in the neck muscles, and torticollis. When this is associated with atrophy of the neck and shoulder muscles, more emphasis should be placed on these symptoms. I shall therefore emphasize, in the diagnosis of tumor of the medulla oblongata, the importance of careful studies for the presence of slight symptoms referable to involvement of the cranial nerves originating in the medulla oblongata in cases that present pain in the neck and shoulder muscles, associated with hypertonic states of the neck muscles.

DISCUSSION

Dr. A. E. Bennett: An almost identical case occurred at the Orthopaedic Hospital on Dr. Sinkler's service. Unfortunately the patient died forty-eight hours after admission and a diagnosis had not been established. She had just had a perineorraphy performed, and an ascending myelitis was considered. She had symptoms similar to those of Dr. Rhein's patient. When she came in she had a diplegia with bulbar symptoms. Lumbar puncture was done in the upright position; within twenty-four hours she developed all the signs of medullary compression and died. At necropsy an endothelioma, springing from the dura, was found in almost the same location as in Dr. Rhein's specimen.

Dr. William G. Spiller: I have seen a few cases of tumor at the foramen magnum or growing through it, in addition to the one reported by Dr. Frazier and myself, to which Dr. Rhein has alluded.

1732 Pine Street.

4. Frey: Ztschr. f. d. ges. Neurol. u. Psychiat. Orig. **21**:131, 1913.

ON THE DEFORMITY OF THE FOOT IN DYSTONIA MUSCULORUM *

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AND
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The comparative rarity of flexor rigidity of the lower extremities in cases of epidemic encephalitis would alone justify a report of two cases showing this deformity. However, our main object is to explain the mechanism of production of the foot deformity of the syndrome of dystonia musculorum, (1) by various distinct muscle groups, and (2) by the two very different processes of contraction and of contracture separated and differentiated one from the other by means of ether anesthesia. Hitherto these deformities have not been decipherable in terms of any stereotyped postures. We shall endeavor to show that this may easily be done.

ONSET AND DEVELOPMENT OF EXTENSOR RIGIDITY OF THE LOWER EXTREMITIES

Both cases were instances of epidemic encephalitis in young girls eventually showing the clinical picture of dystonia musculorum deformans.

CASE 1.—R. E., aged 15, complained of a cold, bronchitis and pain in the chest in October, 1919. These symptoms were followed during the subsequent year by continuation of the pain, drowsiness, diplopia, headache, drooping of the right eyelid and "dragging" of the left foot. On Christmas day, 1920, choreiform movements began in both legs, which prevented the patient from sitting still. Two days later these movements began in the upper extremities, and two days after that in the head and neck. She was admitted to Bellevue Hospital in January, 1920, where she remained five months. There the choreiform movements continuously carried the trunk and extremities into the posture originally described by Sherrington in experimental decerebration at upper pontile levels. She was admitted to Montefiore Hospital Sept. 29, 1921, showing the picture just described.

CASE 2.—J. S., aged 17, complained of tiredness and sleepiness shortly after January, 1920, that is, about the same time as R. E. She could not sleep well. In August she had fever and pains in her legs. In January, 1921, that is about the same time as R. E., movements of the hands, feet and head began, following

* Read at the Forty-Ninth Annual Meeting of the American Neurological Association, Boston, June 2, 1923.

Fig. 1 (Case 1).—At this stage R. E. showed little permanent deformity. Here she was still able to stand assisted.

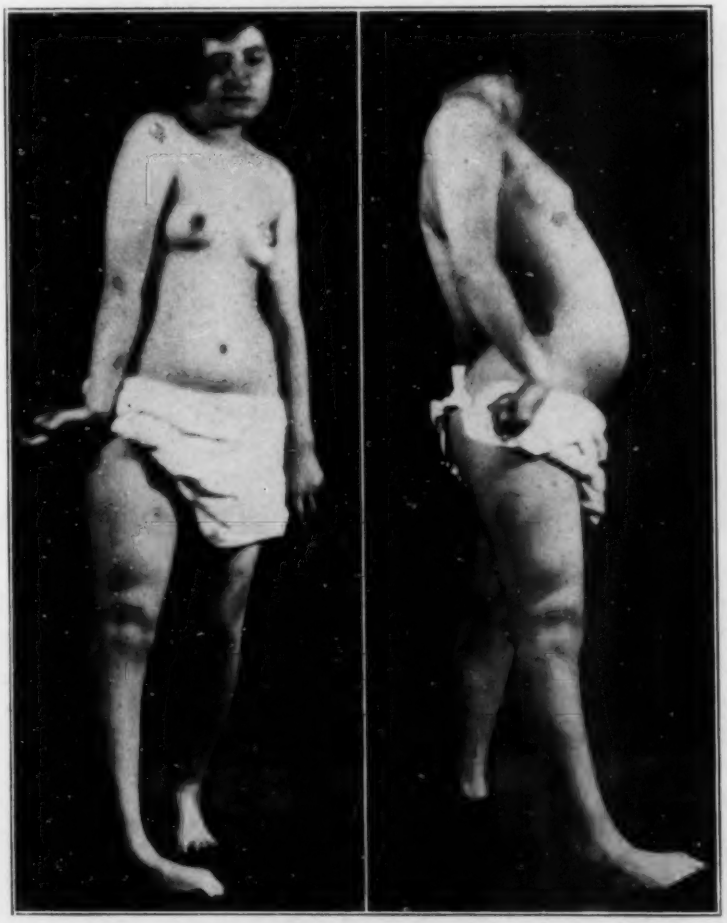

Fig. 2 (Case 2).—The patient is still able to stand alone. Note the ventral foot and extended legs, particularly the right.

a family quarrel and a severe emotional disturbance. Two days later fever and diplopia were present. In May she had an attack of vomiting and abdominal pain. Her pain persisted on and off until March, 1922, when she was admitted to Mt. Sinai Hospital complaining of abdominal pain and mental depression. She became noisy and excited, and occasionally confused at night. She finally left the hospital, but was admitted to Montefiore Hospital, May 13, 1922.

Here examination showed choreiform movements which were like those of R. E., except that at times the muscles involved were not exclusively those active in producing, in the legs, the extensor type of decerebrate posture.[1] This, as the later development of the case showed, was the beginning of the transition to a flexed condition of the legs.

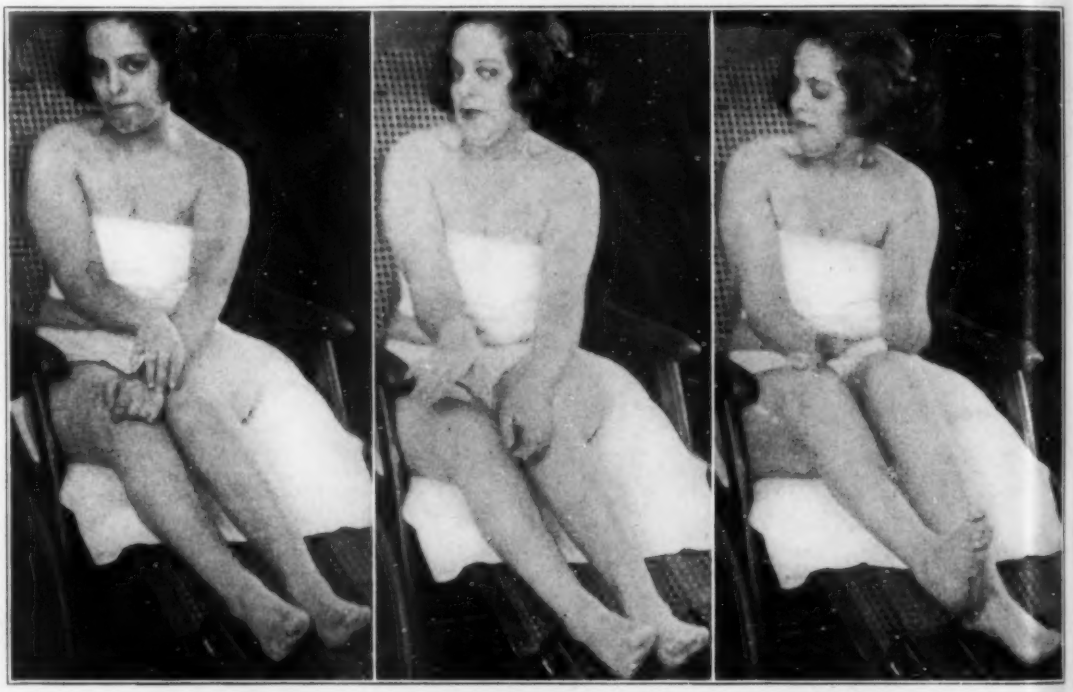

Fig. 3 (Case 1).—These and subsequent photographs are reproductions from a cinematographic film. R. E. in 1921. These show the foot carried by contractions into the posture subsequently maintained by contracture.

In both patients, the movements produced extension of the lower extremities. In both a mild, permanent equinovarus position of the foot with flexion of the toes was present (Figs. 1 and 2). The move-

1. A detailed account of the muscles involved will be found in a paper by W. M. Kraus and A. M. Rabiner, On the Production of Neuromuscular Patterns by Release of Spinal Integrations After Decerebration, J. Neurol. & Psychopath. 3:209, 1922.

ments accentuated this. There was moderate rigidity in both lower extremities. The arm conditions will not be considered at all in this paper since they are not pertinent to this discussion.

THE TRANSITION BETWEEN THE MOBILE AND IMMOBILE PRODUCTION OF THE EXTENSOR POSITION. "THE VENTRAL FOOT"

Moving pictures of R. E. (Fig. 3) taken in February, 1922, show that the movements carried the foot from a position of rest into that just described. The same occurred in J. S. Gradually, however, the feet became rigidly held in that position, though not equally on the two sides. Since the muscles producing that deformity all developed on the ventral aspect of the limb and were all supplied by ventral nerves, we have substituted the phrase "ventral foot" for a lengthy description of movements such as extension at the ankle, adduction at the ankle and flexion of the sole and toes. This phrase indicates very briefly not only the anatomic origin of the causative nerves and muscles, but emphasizes the fact that they constitute the distal part of a definite embryologic group.

THE CHANGE FROM EXTENSOR TO FLEXOR RIGIDITY

During the late summer and fall of 1922, the lower extremities gradually assumed a flexed position. Some choreiform movements in this new direction persisted for some time, but soon disappeared at all joints, except occasionally at the hip, due to their prevention by increasing rigidity. With the exception of the ankle and foot, the *posture* was that seen in paraplegia in flexion (Figs. 4 and 5). We cannot speak of these cases as "para*plegia* in flexion" since there was *no loss of the ability to initiate voluntary power but only almost complete loss of its manifestations due to rigidity*. The suffix "plegia" we feel should be limited to conditions of flaccid paralysis following loss of voluntary power.

The feet, as the photographs show (Figs. 4 and 5) were characteristic of dystonia musculorum deformans, but in no way characteristic of simple "paraplegia in flexion," for in this condition there is no pes cavus, no flexion of the toes, not very much adduction and no extension of the foot (its relation to the anterior surface of the leg is one of an angle of 90, rather than one of 180 degrees as in extensor rigidity, "paraplegia in extension").

The sequence of extensor rigidity followed by flexor rigidity led us to suppose that there remained a residuum of the postural defects of the extensor phase *caused by contracture* which complicated the picture. In brief, the ventral foot persisted in a posture in which contractions

of dorsal muscles control the posture of the foot. The accompanying table shows the leg muscles divided into dorsal and ventral groups. It was our presumption that the muscles of Column B, Group III, remained set by contracture, while the muscles in Column A were being activated

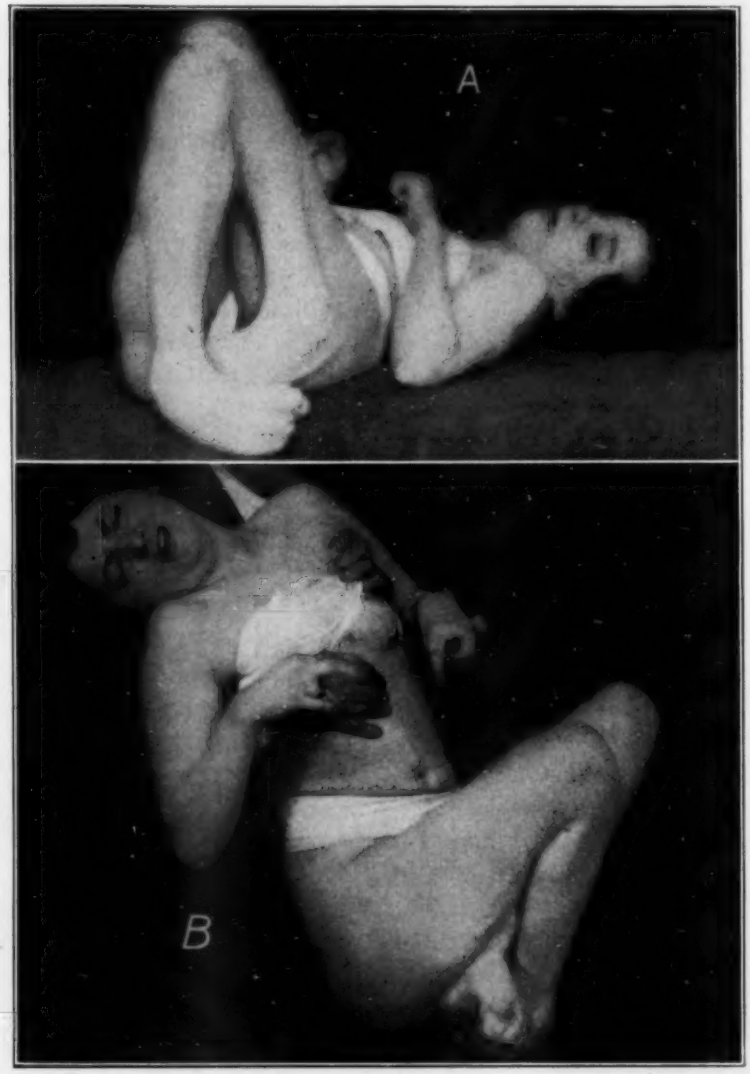

Fig. 4.—*A*, R. E. (Case 1), note the extreme flexor rigidity and the foot deformities. *B* (Case 2), note the extreme rigidity causing the legs to be held in flexion even when the patient is suspended. Note the foot deformities.

by contractions. Were these muscles alone determining its posture the deformity of simple paraplegia in flexion would have been present. It

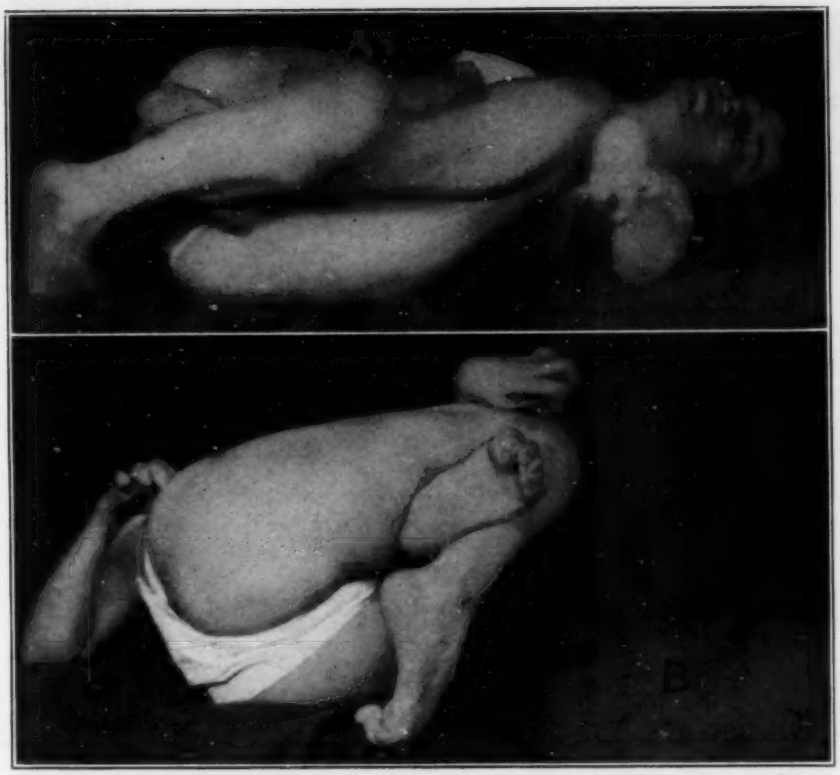

Fig. 5 (Case 2).—*A*, note the extreme flexor rigidity particularly of the left foot and the deformity of the right foot; *B*, note, in addition to the flexor rigidity, the deformities of the right foot, often called the "semilunar foot."

Fig. 6 (Case 2).—Note the flaccidity under anesthesia. The legs are being supported to demonstrate the remaining contractures of the foot muscles. Note also the "semilunar foot" on the left.

was determined therefore to try to separate contracting from contractured muscles by means of ether anesthesia. Figures 6 and 7 show the extreme flaccidity associated with residual flexion of the toes and pes cavus. These positions were quite different from those present when the patients were not under ether. These contractures could only be partially overcome by very forceful traction, while those of the sole and toes could not be overcome at all.

THE RÔLES OF CONTRACTION AND CONTRACTURE

By study of the accompanying table and the photographs it becomes apparent that the contractures of the muscles producing the "ventral foot" quite spoiled the simple picture of the "dorsal foot" of "paraplegia

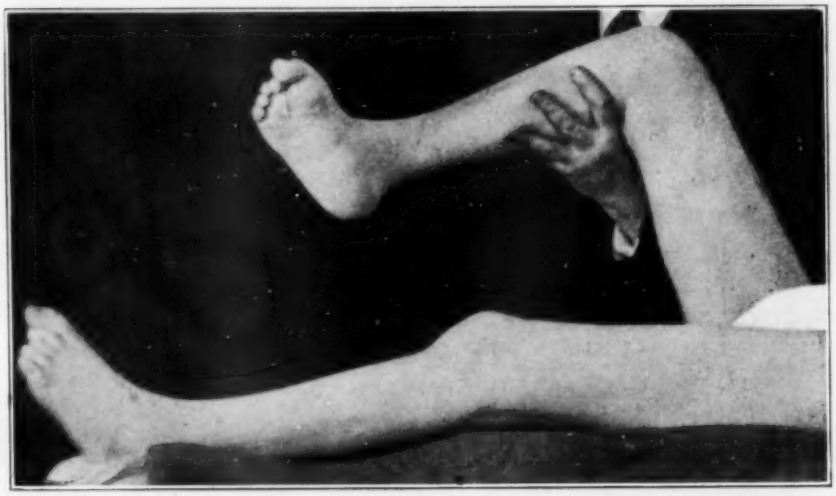

Fig. 7 (Case 2).—Note the flaccidity under anesthesia. The flexion posture is gone, but contracture maintains, pes cavus, flexion of the toes and inversion at the ankle.

in flexion" in which the extensors of the toes are active as well as the peronei and tibialis anticus, which latter balance each other's lateral action (see table). A combined "dorsoventral foot" resulted, whose position as regards inversion was due to the combined action of the tibialis anticus and tibialis posticus. The turning of the sole so that it lay in the longitudinal plane of the leg was facilitated by the position of the foot. It was held by the contractured gastrocnemius on the one hand and the contracting flexor muscles of the ankle on the other, in a position at a little more than a right angle to the leg.

This explanation of the mechanism of production of the foot deformities in the dystonic forms of epidemic encephalitis due to com-

bination of contracture and contraction may be applied to other forms of dystonia musculorum. It is quite apparent that transitional and incomplete varieties of this dorsoventral foot may occur, dependent on the intensity of the contractures and the degree to which the various postural elements composing the classical picture such as flexion, extension, adduction and so forth, at various joints of the ankle and the foot are present. These incomplete and transitional forms must depend on correspondingly incomplete and patchy lesions of the central nervous system.

*The Muscles Active in Flexor Rigidity (A) and in Extensor Rigidity (B)**

Group	A		B	
	Ventral	Dorsal	Ventral	Dorsal
I	†Pectineus (Fl. & Ad. hip)	Iliopsoas (Fl. hip) Tensor fasciae femoris (Fl. hip) Sartorius (Fl. hip) †Pectineus (Fl. & Ad. hip)	Adductors (Ad. hip) Semimembranosus (Ext. hip) Semitendinosus (Ext. hip) Biceps femoris (Ext. hip)	
II	Gracilis (Fl. & Ad. knee) Semitendinosus (Fl. knee) Semimembranosus (Fl. knee) Biceps femoris (Fl. knee)	.....	.....	Quadriceps femoris (Ext. knee)
III	....	Tibialis anticus (Fl. & Ad. ankle) Extensor digitorum longus (Fl. ankle, Ext. toes) Extensor longus hallucis (Fl. ankle, Ext. big toe) Peroneus longus (Ext. Ev. ankle) Peroneus brevis (Ext. Ev. ankle)	Gastronemius (Ext. ankle) Soleus (Ext. ankle) Tibialis posticus (Ext. ankle) Flexor digitorum longus } Fl. toes Flexor hallucis longus... } & Ext. Quadratus plantae..... } ankle Abductor digiti quinti ○ Flexor digiti quinti brevis ○ Opponens digiti quinti Interosseus plantaris 1 Interosseus plantaris 2 ○○ Interosseus plantaris 3 Interosseus dorsalis 1 Interosseus dorsalis 2 Interosseus dorsalis 3 ○○ Interosseus dorsalis 4 Adductor hallucis ○ Lumbricalis 1 Lumbricalis 2 Lumbricalis 3 ○○ Lumbricalis 4 Abductor hallucis ○ Flexor digitorum brevis ○ Flexor hallucis brevis ○	

* This does not account for all the muscles of the lower extremities, since observation or testing of all of them has not been possible. In both A and B, Group I includes muscles acting at the hip, Group II those acting at the knee, Group III those acting at the ankle, foot and toes. Fl., flexion; Ext., extension; Ad., adduction; Ev., eversion; ○, action indicated by the name; ○○, extend toes at interphalangeal joints and flex at metacarpophalangeal joints. Dorsal interossei abduct toes, ventral interossei adduct toes.

† Double muscle. Supplied by both dorsal and ventral nerves.

A COMPARATIVE STUDY OF INTRASPINAL PRESSURE, BLOOD PRESSURE AND INTRA-OCULAR TENSION

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This study was undertaken for the purpose of determining whether a relationship exists between intraspinal pressure, blood pressure and intra-ocular tension. The order of procedure, the posture of the patient, the arm used in determining the blood pressure and the instruments used were always the same. The instruments were the Fleischer spinal manometer, the Schiotz's tonometer and the Baumanometer. The blood pressure was taken on the right arm with the patient lying flat on his back. The systolic pressure was recorded at the first distinct click, and the diastolic pressure at the point where the sharp snappy knock changed into a dull blow; i. e. at the first and fourth phases, respectively. The ocular tension was taken in the same posture after the use of 1 per cent. holocain solution. The spinal pressure was taken with the patient lying on the left side and after the use of 1 c.c. of 2 per cent. procain solution. The blood pressure, intra-ocular tension, and intraspinal pressure were recorded consecutively in 100 cases.

When considered as a whole, no definite parallelism exists between the systolic, diastolic or pulse pressure and the intra-ocular tension and intraspinal pressure, although there seems to be a tendency for them to rise or fall together. The lack of parallelism may be explained by various factors which exert a more marked influence on one form of pressure than another. It is probable that the ocular pressure and spinal pressure have a tendency to adjust themselves to conditions which tend gradually to disturb their normal balance. The highest spinal pressure occurred in fracture of the skull, convulsions, meningitis, chronic nephritis, cerebral hemorrhage and cerebrospinal syphilis, without however a proportionate rise in blood pressure or ocular tension. The highest ocular pressures occurred in glaucoma, brain tumor, postpartum cases, cerebrospinal syphilis, arteriosclerosis and cerebral hemorrhage.

In Table 1 a comparison is made of the groups of high and low pressures. The average of all 100 cases is given on the top line for the purpose of comparison. If we consider all cases in which the ocular pressure is 20 or over and compare them with all cases in which the ocular pressure is 10 or less we find that the average blood pressure

and spinal pressure are higher in the former group. If we compare all cases in which the spinal pressure is 16 or over with all cases in which the spinal pressure is 7 or less, we find the blood pressure and ocular tension are higher in the former group.

Again, if we take all cases in which the systolic blood pressure is 180 or over and compare them with all of the cases in which the systolic blood pressure is 110 or less, we find that the average ocular tension and average spinal pressure are distinctly higher in the former group.

Although these end-results in each series show that a definite average relationship exists, this does not hold true in individual instances on account of the fact that local conditions may materially raise one type of pressure without showing a reaction on another system. For example, in glaucoma the intra-ocular tension is high, although the systolic blood pressure in one case was only 100 and in another 150,

TABLE 1.—*Comparison of High and Low Pressures*

Number of Cases		Blood Pressure			Ocular Pressure	Spinal Pressure
		Systolic	Diastolic	Pulse		
100	Average of all cases	143.15	88.85	54.10	16.81	12.24
13	Ocular tension, 20 or over	156.54	99.61	56.70	23.77	11.54
11	Ocular tension, 10 or less	121.0	76.0	45.0	8.13	9.0
22	Spinal pressure, 16 or over	162.5	102.27	60.68	18.16	24.23
22	Spinal pressure, 7 or less	118.18	74.54	43.63	15.29	4.95
19	Blood pressure, systolic, 180 or over	209.2	125.8	83.4	18.2	16.6
22	Blood pressure, systolic, 110 or less	103.63	67.27	36.36	14.98	10.7

with spinal pressures of 12 and 8, respectively. In one case of acute meningococcic meningitis the spinal pressure was 32 while the blood pressure was only 105 and the ocular tension was 16. In fracture of the skull the spinal pressure was usually high and the ocular pressure showed a high average; while the blood pressure was below the average, probably owing to shock.

In seventy-five cases all readings were repeated after the removal of spinal fluid; they showed a slight fall in the systolic, diastolic and pulse pressure, and a minute rise in the ocular pressure, and of course a fall in the spinal pressure. When we compare the average for forty-five cases in which 5 c.c. or less of spinal fluid was removed with the average of thirty cases in which 10 c.c. or more was removed the effect on the systolic pressure, diastolic pressure, pulse pressure and ocular tension was a greater fall with the greater amount removed. However, these results were not uniform and, especially when small amounts were removed, there was often a rise in blood pressure and ocular tension, although when larger quantities of spinal fluid were

removed there was a more frequent fall and the average fall in the blood pressure and ocular pressure became greater. We were inclined to think that increases in blood pressure after removing the spinal fluid were due to emotional disturbances in the patients. The changes in ocular tension following lumbar puncture were so slight that they might be interpreted as possible variations in reading the deviations.

As to the effect of removal of spinal fluid on the spinal pressure in seventy-five cases, an average of 7.9 c.c. was removed producing an average fall of 7.0 mm. of mercury, or a little less than 1 mm. for each cubic centimeter withdrawn. This ratio held practically true both when large and small amounts of spinal fluid were withdrawn.

TABLE 2.—*Groups of Diseases*

Number of Cases		Blood Pressure			Ocular Tension	Spinal Pressure
		Systolic	Diastolic	Pulse		
100	Average	142.9	88.8	54.1	16.8	12.24
7	Hemorrhage, cerebral	190	115.7	74.3	17.6	18.3
2	Arteriosclerosis	200	120	80	23	14
4	Hypertension	202.5	117.5	85	18.4	12.5
10	Nephritis, chronic	182.5	114	68.5	15	16.4
17	Cerebrospinal syphilis	147.3	97.4	49.9	17.5	13.6
11	Fractured skull	122.7	74.5	48.2	18.5	16.9
1	Brain tumor	120	90	30	28	14
1	Meningitis, meningococcic	106	70	35	16	32
2	Glaucoma	125	80	45	31	10
7	Pregnancy	135.7	89.3	46.4	18	10.4
11	Postpartum (normal)	118.5	77.3	41.2	16.8	6.2
5	Postpartum (toxic)	178	114	64	18.8	11.8
4	Epilepsy	107.5	62.5	45	12	9.7
3	Psychosis	115	76.6	38.4	15.8	11.3
1	Hysteria	135	90	45	17	8
3	Pneumonia	130	70	60	12.6	11.3
2	Influenza	115	70	45	12.5	7
4	Bronchitis, acute	115.3	73.8	41.5	12.7	10.2
2	Tuberculosis, pulmonary	120	85	35	17	8.5
1	Carcinomatosis	110	60	50	17	14
1	Pituitary dystrophy	110	70	40	11	7
1	Pelvic peritonitis	130	75	55	16	2

When we consider groups of diseases (Table 2) we find that in cerebral hemorrhage, hypertension, arteriosclerosis and chronic nephritis, all of which showed a high average blood pressure, the spinal pressure was above normal and above the average, while the ocular pressure was above our average in all except chronic nephritis. In eleven cases of fracture of the skull, although the blood pressure was below the average, the spinal pressure was above normal and above our average and the ocular pressure was above the average. In seventeen cases of cerebrospinal syphilis the systolic blood pressure, ocular pressure and spinal pressure were above the average.

We thought it probable that the increased abdominal pressure in pregnancy would produce an increased intracranial pressure and therefore a rise in intraspinal pressure. To determine this point we examined seven cases of pregnancy in the ninth month and compared these with eleven uncomplicated postpartum cases and five toxic postpartum cases

(nephritic or eclamptic or both). In pregnancy the average blood pressure was above normal but below our average, the ocular pressure was above our average and the spinal pressure was below our average but slightly above normal. In normal postpartum cases the blood pressure and spinal pressure were below the average while in the toxic postpartum cases the blood pressure and ocular tension were above the average while the spinal pressure was above normal but below our average.

In four cases of epilepsy in which observations were made in the interval between convulsions, the blood pressure and ocular tension were below normal and below the average, and the spinal pressure was below our average but within normal limits.

In a case of cerebral hemorrhage the spinal pressure was 30 mm.—forty cubic centimeters of 30 per cent. sodium chlorid solution was given intravenously and readings were repeated every five minutes; they showed a gradual fall in thirty-three minutes to a spinal pressure of 4 mm.

In a case of uremic convulsions, the spinal pressure fluctuated betweeen 60 and 80 mm. during the convulsion, but fell to 30 mm. after the convulsion was over. In another case of uremic convulsions the pressure rose to 47 during the convulsion but fell to 7 mm. after the convulsion was over. During stertorous respiration the pressure was 2 mm. higher during inspiration than during expiration; during sleep it fell to from 1 to 3 mm., but rose to 10 mm. when the patient was awakened artificially.

In a case of brain injury the spinal pressure fell from 28 mm. to 10 mm. after the administration of sodium chlorid by mouth.

CONCLUSIONS

1. No individual parallelism exists between intraspinal pressure, arterial pressure and ocular tension.

2. On an average, a high pressure of one type is associated with a high pressure of the other types; the same is true of low pressure.

3. In certain diseases, essentially local conditions may cause a high pressure without apparent influence on other forms of pressure.

Critical Reviews

THE MECHANISM OF SPLANCHNOGENIC PAIN

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Certain symptoms are frequently observed which, originated by visceral disturbances, manifest themselves in those regions of the external surfaces of the body whose central innervation is more intimately related with that of the affected viscus. In many cases such zones include the external projection areas of the responsible internal organ, but in others the symptoms just mentioned are referred to cutaneous territories rather distant, and without apparent relation to it.

The existence of those two groups of cases is explained by the anatomic connections between the neurons of the sympathetic ganglia of the lateral chains and those of the spinal centers from which the nerve roots emerge at each vertebral level. Another factor in this explanation is that the metameric segmentation of the body, although very striking in the embryo and resembling the almost complete segmentation of the primitive vertebrates like the amphioxus, is still present in the adult. In the latter, however, certain segments appear rather modified and displaced, but not to the extent that each viscus fails to receive its innervation from the same parts of the center supplying the skin and muscles of the respective metameres.

We are indebted for the knowledge of the visceral origin of those different manifestations to the remarkable clinical investigations of Head [1] and Mackenzie.[2] To the latter we also owe an explanation of their mechanism, apparently admitted by the vast majority. It is only fair also to quote the earlier suggestions of Sturge [3] and Ross [4] on the subject.

Head, in 1893, had already recognized two types of pain of visceral origin: "one in the organ itself, which is more that of discomfort, and another in the surface of the body, which is a real painful sensation." He laid down the law of the location of visceral pain as follows:

1. Head, Henry: On Disturbances of Sensation with Special Reference to the Pain of Visceral Disease, Brain **16**:127, 1893.

2. Mackenzie, James: Diseases of the Heart, Oxford University Press, 1918; Symptoms and Their Interpretation, New York, Paul B. Hoeber, 1920.

3. Sturge, W. A.: The Phenomena of Angina Pectoris, and Their Bearing Upon the Theory of Counter Irritation, Brain **5**:492 (Jan.) 1883.

4. Ross, James: On the Segmental Distribution of Sensory Disorders, Brain **10**:350 (Jan.) 1888.

"Where a painful stimulus is applied to a part of low sensibility in close central connection with a part of much greater sensibility, the pain produced is felt in the part of higher sensibility, rather than in the part of lower sensibility to which the stimulus was actually applied." The diagrams and tables of this author are considered classical.

Later, Pottenger, on calling attention to some visceromotor and viscerotrophic reflexes, added new facts of interest [5] which, compiled and fully discussed, form the subject matter of a recent monograph.[6] In this, as in the works of the two investigators already mentioned, one may study in detail and with advantage the two groups of the "viscerogenic" symptoms [7] that I have referred to. Such symptoms might be placed in three classes: sensory, motor and trophic. This paper, however, will deal exclusively with those of the first class and a discussion of their peculiar mechanism.

THE VISCEROSENSORY REFLEX

To explain how pains of that nature are produced, Mackenzie evolved the notion of the visçerosensory reflex. Taking into account that the reflex phenomena originating in all organs, and especially in the hollow viscera, are greatly similar in origin and character, in spite of differences in form and function, and emphasizing the fact of the insensibility of the viscera to ordinary stimuli of touch, temperature, trauma, etc., he considered it necessary to find an explanation for the production of splanchnogenic pain, differing from that usually given for the pain caused directly by external stimuli. In fact he admitted [8] that:

"From the viscus, an abnormal stimulus is conveyed by the sympathetic nerves to the spinal cord. On reaching the cord the abnormal stimulus spreads beyond the sympathetic center and affects nerve cells in its immediate neighborhood. The cells so stimulated react according to their function, the sensory causing a sensation which the brain recognizes as pain and refers to the peripheral distribution of the sensory nerve in the skin or muscles, the motor

5. Pottenger, F. M.: A New Physical Sign Found in the Presence of Inflammatory Conditions of the Lungs and Pleura, J. A. M. A. **52**:771 (March 6) 1909; Muscle Spasm and Degeneration, St. Louis, C. V. Mosby Co., 1912; Spasm of the Lumbar Muscles. A Diagnostic Sign in Inflammation of the Kidney, J. A. M. A. **60**:980 (March 29) 1913; The Significance of Limited Respiratory Movement and Visceromotor, Viscerosensory and Viscerotrophic Reflexes in the Diagnosis of Pulmonary and Pleural Inflammation, Am. Rev. Tuberc. **2**:734 (Feb.) 1919.

6. Pottenger, F. M.: Symptoms of Visceral Disease, St. Louis, C. V. Mosby Co., 1919.

7. The word "splanchnogenic" is preferable to the hybrid word viscerogenic.

8. Mackenzie, James: Diseases of the Heart (Footnote 2), p. 60; Symptoms and Their Interpretation (Footnote 2), p. 76; Angina Pectoris, Oxford University Press, 1923, Figure 4.

producing contraction of the muscles. The abnormal stimulation may leave a portion of the cord abnormally irritable so that the tissues supplied by nerves from that portion of the cord are hyperalgesic, and attacks of pain, as angina pectoris, are more easily provoked."

Such an explanation, as attractive as it is simple, seems to have satisfied clinicians. Pottenger,[6] for example, says:

"Sensory sympathetic fibers are found along with the motor sympathetic fibers in all structures, and when irritated the impulses are carried centralward where they are transferred to other neurones to complete reflexes in the skeletal structures. Therefore, every organ may generate stimuli which, if sufficiently strong, coursing centralward through the sympathetics, may result in reflex action in the skeletal structures through the spinal nerves which supply them. From physiologic facts we are led to assert that every important internal viscus is connected in the central nervous system through afferent *sympathetic* and efferent spinal nerves with definite skeletal structures, and if inflamed, should show reflex sensory and motor activity; and if the inflammation becomes chronic, trophic changes should also be manifested. Therefore, spasm of muscles, altered cutaneous sensation and degeneration of muscles, subcutaneous tissue and skin, become important diagnostic phenomena."

These conclusions Pottenger adheres to, yet admits that the soundness of the principles based on the physiologic facts to which he refers, is still rather disputed.

On the one hand the diagram of Langley,[9] based on interesting experiments with nicotin, a substance having the peculiar property of paralyzing only the synapses of the sympathetic cells and leaving intact the conductivity of the sympathetic visceroperipheral fibers, shows that all the afferent tracts run without interruption to the posterior root ganglia and never come into direct relation with the sympathetic ganglia. Therefore, the stimuli conveyed through these tracts reach the cerebrospinal centers before they can possibly be referred toward the periphery. This opinion is shared by Gaskell:[10] "The course of the sensory fibers is the same in all sensory nerves, viz., direct to the cells of the posterior root ganglia, with no connection with any cells in the sympathetic ganglia; the so-called sympathetic system is not a complete central nervous system but consists purely of excitomotor neurons."

On the other hand, Bechterew,[11] faithful to the experiment of Claude Bernard on the lingual nerve, later satisfactorily explained by Langley, believes that the sympathetic ganglia possess the functions of real reflex centers: "the sensory sympathetic fibers transmit impressions to the

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9. Langley, J. N., cited by Cajal: Histologie du système nerveux d l'homme et des vertebrés, Paris **20**:202, 1909; Autonomic Nervous System, Cambridge, 1921, p. 5.

10. Gaskell, N. H.: The Involuntary Nervous System, New York, Longmans, Green & Co., 1916, p. 17.

11. Bechterew, W. V.: Les fonctions nerveuses, Part 1, Figure 13 *gs*.

spinal cord and brain, the motor fibers supply the involuntary or unstriped musculature; the sympathetic system is also, without doubt, operative in originating many reflexes in the sphere of the internal organs."

This idea is made to appear as a consequence of Ramon y Cajal's conceptions of the cellular interruption of the nerve fibers in the sympathetic ganglia as well as in the other system. It is certainly strange to infer from such a conception that the ganglia mentioned possess the function of reflex centers. I find, on the contrary, that such an interpretation is opposed to the following physiologic conclusions, with which the Spanish investigator sums up his exhaustive work: [12]

"According to Langley's physiologic diagram, we can consider the great sympathetic as a motor system exclusively, controlled by the cord and having the function of coordinating the automatic movements of intestine, blood vessels, excretory ducts, glands, and muscles of the hairs. And since sensory cells have not as yet been discovered in the great sympathetic, it is absolutely necessary to admit, according to Koelliker, that the sensory stimuli bound from the mucous membranes to the spinal cord travel through the fibers of the posterior root ganglia. For the heart, stomach, etc., these fibers form part of the vagus; for other organs, of the trigeminus, etc. Having reached the cord, at a nucleus as yet undetermined, and which is called theoretically the motor sympathetic nucleus, the centripetal stimuli become centrifugal or motor. The tracts through which the latter are covered are composed, according to Langley's conception, of two successive neurons: the first is located in the cord, and its axis cylinder, Langley's preganglionic fiber, terminates in the ganglia belonging either to the great sympathetic or to the intestines or even to the glands; the second, which is the real sympathetic neuron, is situated in the ganglia of the various organs that we have just mentioned, and sends the terminal arborization of its axis cylinders to the muscular fibers of intestines, glands, blood vessels, etc."

On the other hand, Bechterew's physiologic conclusions, which, as has been seen, clinicians seem to have accepted up to now, are anatomically based on the sympathetic sensory neuron, which Dogiel claims to have discovered.[13] According to this histologist "the sensory neuron gathers through its dendrites visceral stimuli and transmits them by way of its axis cylinders to Auerbach's and Meissner's ganglia, to the solar ganglia and to those of the gallbladder, and finally of the great sympathetic, where on reaching the motor neurons, they are reflected and converted into motor impulses. In this way the viscera would be supplied at the same time by two sympathetic systems: by the lesser system, accepted by Dogiel, in which the dendrons of the sympathetic sensory neurons would gather the visceral stimuli; and by the greater system, universally accepted, in which those impressions

12. Cajal, S. R. y: Histologie du système nerveux de l'homme et des vertébrés (Footnote 9).

13. Dogiel, cited by Cajal: Footnote 12 **20**:920, 921 and 942.

stimulate the ends of the fibers of the posterior root ganglia. In the lesser system, the reflex motor stimulus is produced by the sympathetic motor neuron; in the greater system, such stimulus comes from the latter neuron and from the motor spinal cells."

But Cajal believes that Dogiel's conception is a mere hypothesis, which to be tenable would require the previous confirmation of the existence of the sympathetic sensory neuron described by the Russian investigator. This has as yet not been accomplished. The results of Cajal's, Koelliker's and Villa's researches, carried out both with Ehrlich's and Golgi's methods, have been totally negative.

As can be seen, the prevailing explanation of the clinical phenomena brought about by visceral disturbances rests on a rather inconsistent anatomicophysiologic basis.

PHYSIOLOGY

It is difficult to understand why the ideas of the two Russian investigators should have influenced clinicians, and especially the Anglo-Saxons, to a greater extent than have the views of English physiologists and of the Spanish histoneurologist. Possibly the apparent simplicity of Mackenzie's diagram was a great factor in their predilection. It has seemed easier to conceive of a complete reflex arc within the vegetative system, including a sympathetic afferent tract, to explain visceral manifestations in the somatic sphere. But the ease of such an explanation is only imaginary, from an anatomic point of view, since it introduces a complicating element, the hypothetical sensory neuron, which is unnecessary in the physiologic scheme. This scheme may be explained by anatomic facts almost universally accepted. Besides, phenomena seem to take place in the organism with greater complexity than are indicated by Mackenzie's diagram. Physiologists, and even at times clinicians, are capable of detecting this before the histologic facts are revealed, as has occurred in the present case with Langley's and Gaskell's experiments and the findings of Cajal.

I believe that the arduous and fruitful work of the latter has not as yet received the clinical recognition it deserves. Conceptions and interpretations prevail in recent textbooks which are untenable in the light of certain facts demonstrated long ago. The discontinuity or independence of the neurons, the economic laws of their transmitting protoplasm and of the time of transmission, together with the dynamic polarization in all these, are principles which should serve constantly to guide the neuropathologist in explaining morbid phenomena.

The centripetal tract is common to both nervous systems. It is composed of the medullated fibers that reach the posterior root ganglia, carrying the impulses proceeding not only from the external wall of the body but also from within. The former are the results of the trans-

formation in the terminal end plates of physical stimuli: either vibratory: heat, light, electricity, sound; or nonvibratory: touch, impact, pressure, trauma, etc. The inner impulses are mostly generated by chemical stimuli: intestinal contents, secretions, excretions, blood, lymph, plasma, etc.; these stimuli, like the previous ones, cause corresponding reactions. Initiated in the nerve cell bodies, all these reactions, when conveyed by the centrifugal tracts, may travel either to the cerebrospinal paths, or to the vegetative system; but those that emerge from the sympathetic ganglia, destined for the viscera, are conveyed by nonmedullated fibers.

The centrifugal fibers, therefore, are of two structural types instead of one, as in the afferent tract. Now, since [14] "each neuron is connected to a considerable number of others by the innumerable ramifications of their protoplasm and axis cylinders, each stimulus received in the periphery is propagated in a fan-like manner, involving as it progresses each time a greater multitude of neurons. . . . But the latter, due to the diversity of their locations and relations, are crossed by currents of different nature and quality, their different *shapes* thus influencing the intensity, direction and manner of distribution of the nervous wave." As Gaskell [10] also states, the great physiologic problems cannot be solved in a satisfactory manner without the aid of morphology. In the particular problem that I am now considering, namely, the conduction of nerve energy, we deal with two types of centrifugal fibers, medullated and nonmedullated. To such a great structural variation should necessarily correspond an important difference in the manner of transporting energy, which is the actual function of the fibers. The complex structure of the myelin sheath, which serves both as a support to the axis cylinder in its axial position, and as an isolator of currents, is not indispensable to the simple function of the fibers, since those of Remak do not possess it; but the myelin sheath means for the nervous system "a functional improvement, phylogenetically contemporary with the vertebra, which appears in greater abundance the higher the nervous system is developed and the more varied its relations with a more diversified environment." On the other hand, "while embryonic or young, functioning only for the primitive internal life of invertebrates or inferior vertebrates, these fibers remain nonmedullated, either for economy or because they perform other functions, like those in the sympathetic, or even because being of shorter length the risk of loss of currents is less serious.[15]" Perhaps also, it might be said, because the manner of propagation of nerve impulses is different in these fibers. With such an assumption the loss of currents would be

14. Cajal, S. R. y: Cited in Footnote 12 **20**:106 and 137.
15. Cajal, S. R. y: Cited in Footnote 12 **20**:276.

of no concern; just the opposite, we should consider advantageous the relative shortness and bareness of the fibers for a larger field of action of the propagated energy.

In the transmission through medullated fibers it is essential that there should be no loss of current, since the impulses thus conducted, originating in a particular peripheral point, go to stimulate through the corresponding body cells other definite parts, either of the psychic realm or of the voluntary muscular system. Take, for example, any tendinous or cutaneous reflex elicited clinically. In the transmission through nonmedullated fibers, which are all centrifugal and destined to the vegetative system, it seems useful for the maintenance of intervisceral sympathy that the nervous discharge may find its way either through one fiber or through any of the neighboring ones. In this way the discharge may leave during its course a certain amount of influence in those organic territories at that moment in closer functional relation with that organ for which the impulse was primarily destined. This is favored by the peculiar structure of the sympathetic system, which as we know is characterized by intricate plexuses and disseminated ganglia. The successive repetition of the innumerable possible combinations in the direction and distribution of nerve charge in the sympathetic system should sustain in it a potential, the equilibrium of which would be established, destroyed and reestablished continually. These variations in the potential would be caused by the stimuli in the nerve cell bodies exerted on their initial charges, which in turn would be the chemical energy of the circulating plasmas transformed by the neurons themselves. It could be said that the impulses transmitted by the medullated fibers are individual or specific, but that those transmitted by the fibers of Remak are general or indifferent; moreover, that in the former the changes of nerve potential manifest themselves as currents, similar to those of the electric batteries, to which M. Márquez [16] many years ago compared the neurons; and in the latter the changes would be accomplished by real discharges, like condensers, preferring, like atmospheric electricity, not any preestablished direction, but all those offering best conduction.

The ganglia of the intravisceral plexuses located in great numbers in the vicinity of epithelial and smooth muscle elements, whose function they control, would coordinate autonomically the direction and intensity of the charges required by them during each functional phase. They would not act as real reflex centers, but as maintainers of the equilibrium of the tension between the epithelial and muscular cells, broken almost continually by the consumption of energy of both during the harmonious work of the respective visceral regions.

16. Márquez, Manuel: Algunas aplicaciones de la nuevas ideas sobre la estructura del sistema nervioso, Madrid, 1898.

There would then always exist in the vegetative system a state of tension which, like all biologic functions, might oscillate within certain normal limits, changing locally according to the needs required by the work of the organs, whose functional automatism would in such a way be actually secured.

The intermittent appeals of the viscera, due to their specific stimuli adapted both in quantity and quality, carried by the centripetal fibers to the posterior root ganglia and the spinal centers, would cause useful variations in the state of tension of the corresponding part of the sympathetic system, through the chain which, beginning in the preganglionic neurons, continues through the postganglionic and the autonomic of the peripheral ganglia up to the interstitial neurons.

This conjecture finds anatomic basis in the diversity of the types of neurons of the plexuses: stellate cells or cells of long ramifications, cells of short ramifications or Dogiel's cells, interstitial cells of Cajal; all distributing motor charges. Also physiologic support in certain facts, for instance, that "the effects of electrotonus, which appear to be due to a phenomenon of polarization of the medullated nerve, are not observed in those which lack the myelin sheath or have lost it by degeneration." [17] And furthermore, in the experimental study of nerve conduction which has led Keith Lucas [18] and others to infer that the progression of the transmitted impulse depends more on the energy derived from a source distributed along the conducting fiber than on its initial energy. Lucas said:

"The whole body of evidence is, I think, sufficient to justify the conclusion that nerve uses oxygen and gives off carbon dioxid when it is conducting nervous impulses. This confirms the inference from Adrian's experiments that the nervous impulse depends for its transmission on the supply of energy by the nerve itself along its course. If this view is correct, we may be justified in supposing that by its very nature the nervous impulse is dependent for its intensity only on the conditions which it encounters during conduction, not on the intensity with which it is initiated. This at any rate seems to be the hypothesis which best accords with the experimental facts at present known."

Additional data in recent literature may also be quoted. By observing the development of organisms through the forms with purely vegetative functions to the more highly organized types with dual systems, Lenaz [19] makes clear the relation between the vegetative and the sensorimotor systems of innervation. He admits that, like other

17. Ocana, J. G.: Fisiologia humana teórica y experimental, Madrid **1**:9, 1904.

18. Lucas, Keith: The Conduction of the Nervous Impulse, New York, Longmans, Green & Co., 1917, pp. 8, 22, 23 and 26.

19. Lenaz, L.: The Rôle of the Vegetative Nervous System in Physiology and Pathology. Abstracted in Inst. Med. & Surg. Survey of the American Institute of Medicine, Inc. **3**, Sect. 6, 6, 1922.

organs, the psychic centers are subject to the influence of the vegetative center, and in turn influence physicochemical conditions; he explains the facts as results of changes of excitation within the central apparatus of the vegetative nervous system. These changes may manifest themselves in all organs connected with this system, for instance in the glands and muscles, and also in the organs of conscious thought.

For Schafer,[20] the rule of antagonistic reciprocal innervation in voluntary muscles applies equally to the vegetative centers: intracentral and peripheral centers are entrusted with this reciprocal relation. "Experiments have shown that the effect of stimulation of the vagus or of the sympathetic is determined by the inorganic electrolytes contained in the end-organs. Calcium in excess makes the heart more sensitive to sympathetic action, and accumulation of potassium to vagus stimulation. The effect on the nerve would be due to intracardiac hormones freed during stimulation of those nerves. The production of the hormones is regulated by the vegetative nervous system through the endocrine organs, the vegetative stimuli through internal secretion being modified both by peripheral and by central factors. The reciprocal action of atropin and cholin, an internal secretion of the intestine, are thus explained. Atropin stimulates Auerbach's plexus if there is but little cholin, but reduces the activity of the intestine if there is much of the latter substance." As Arai [21] states, according to Magnus and his co-workers, cholin is in fact the natural hormone for intestinal movement, and a lowering of its production, or of the intestinal sensitiveness to it, would result in a condition of stasis.

Garrelon, Sautenoise and Tinel [22] have recently found that variations in vagosympathetic equilibrium are the necessary conditions of all reactions having an anaphylactic nature. They consider it probable that through similar changes the action of cold, fatigue and other factors in endocrine disturbances take place.

Daniélopolu [23] has recently made known that "very weak doses of epinephrin injected intravenously produced an abdominal vasodilatation; large doses cause a central vasoconstriction and peripheral dilatation, and still higher doses a general vasoconstriction which is more marked in the center than in the periphery. Small doses also slow the heart

20. Schafer, Harry: The Vagus and Sympathetic Systems. Abstracted in Inst. Med. & Surg. Survey of the American Institute of Medicine, Inc. **4**, Sect. 6, 2 (July) 1922.

21. Arai, K.: Choline as a Hormone for Intestinal Movements, Arch. f. d. ges. Physiol. **193**:359, 1922; abstr., J. Nerv. & Ment. Dis., September, 1923.

22. Garrelon, L.; Sautenoise, D., and Tinel, J.: The Relation of the Vago-Sympathetic System to Anaphylaxis and Intoxication, Presse méd. **31**:323 (April 7) 1923.

23. Daniélopolu, D.: Les epreuves végétative, Presse méd. **31**:649 (July 25) 1923.

rhythm and larger ones accentuate it. This effect shows that epinephrin is an amphotropic substance with a sympathetic predominance, and that very small doses stimulate the vagus. Eserin and calcium salts are also amphotropic; also atropin, but the effect on the parasympathetic predominates to such an extent that the effect on the sympathetic may be neglected in practice."

Patterson,[24] from his experimental work arrives at the conclusion that the physiologic readjustment of the vagotomized lung is brought about through some plastic activity of its peripheral neuromuscular mechanism.

Now, concerning the relationship between the sympathetic and endocrine systems, I might quote Pachon's conclusions in his recent report to the last French medical congress.[25] Numerous experimental facts are contrary to the conception of a neuroglandular system in which the sympathetic and endocrine glands were intimately related, and in which the former were controlled by the latter. In their mutual relationship all would be limited by reciprocal interfering actions. Furthermore, Laignel-Lavastine,[26] sharing the same view, adds that the sympathetic is far from having internal secretions as the only stimuli. In his opinion, the action of the sympathetic on the latter is simply a part of the nervous regulation of nutrition in general. He finds anatomicophysiologic support in the belief of the French school, and also of Langley, in a motor visceral vagus considered as a bulbar division of the regulating system of nutrition.

PATHOLOGY

The normal reactions of the silent inner life thus interpreted, it is possible to understand how the abnormal reactions manifest themselves in the external surface, without having recourse to the hypothesis of a sympathetic sensory neuron.

To any stimulus, inappropriate in quantity or quality, the viscus should respond with an exaggerated reaction; that is, with an overexertion. After a period of hyperexcitability, if the stimulus persists, there is first fatigue, which in the muscles expresses itself as spasm or contracture, and later functional insufficiency, temporary or permanent. At all events, the moment arrives when the nerve energy supplied to the affected organ cannot be totally or partially dissipated. Consequently a state of hypertension follows in the corresponding portion of the sympa-

24. Patterson, F. L.: The Readjustment of the Peripheral Lung Motor Mechanism After Bilateral Vagotomy in the Frog, Am. J. Physiol. **8**:189, 1921.

25. Pachon, V.: Considérations physiologiques sur les rapports functionelles du sympathique et des glandes endocrines, Presse méd. **31**:862 (Oct. 13) 1923.

26. Laignel-Lavastine: Part of a Discussion at the Eighteenth French Congress of Medicine, Presse méd. **31**:964 (Oct. 13) 1923.

thetic tract. For a certain length of time, or if the stimulus was not very intense or too unfamiliar, compensating discharges in other parts of the same or other portions are sufficient to dissipate the distorted energy. In other instances, other sympathetic mechanisms, as the vasomotor or the cutaneous glandular, are those that act as safety valves for the excessive tension due to the visceral conflict. But on other occasions, when the suddenness or great intensity of the stimulus appears to be the predominating factor, the balance of tension cannot be reestablished before the accumulation of the centripetal energy in the corresponding spinal centers. In such case, the energy, intensified by the extraordinary number of stimuli coming from the affected viscus and obstructed in its natural course to the sympathetic tract by the hypertension already existing in the latter, raises in turn the potential in the somatic centripetal paths. That increase in potential can only then be used in overexciting either the voluntary motor tract, producing spasm of variable intensity and duration (Mackenzie's visceromotor reflex); or the sensory tract, up to the point of causing through the ascending paths painful sensations, referred by the brain to the respective zones of the nervous peripheral distribution, as if they originated directly from the latter (Mackenzie's viscerosensory reflex). The remaining disturbances in the inner lining of the body or in the parenchymas, caused by the foreign agent, become sources of abnormal stimuli which, if persisting, bring about manifestations of different character in the external body wall; hyperalgesic zones, with or without underlying spasm, regional vasomotor, secretory, or trophic disturbances. It goes without saying that the mechanism of opposite reactions, that is from the external surface of the body to the viscera, does not have to be modified.

The valuable clinical observations of Head, Pottenger, Mackenzie, and others, are in this way more satisfactorily explained. They lose nothing in exactness, and gain much in foundation. Besides, some objections opposed to their current interpretation are thus eliminated. For instance, regarding the chronic precordial pains of cardiac valvular diseases, Esmein [27] writes as follows:

"This interpretation (that of Mackenzie) is certainly ingenious and attractive, but open to some objections. One main objection would be that as the inflammation of the internal organs is above all that which stimulates their nerves to react, it is difficult in a case like the one referred to (a chronic endocardial lesion accompanied by acute prolonged pain) for the heart to be in a state of continual inflammation for a period of thirty-one years. I believe, therefore, that it is necessary to bring in another factor, the distention of the heart. Every time I have observed an individual suffering with such chronic precordial pains, there have been signs of cardiac decompensation, and especially a great dilatation of the heart. Whenever I have succeeded in making it regress,

27. Esmein, C. H.: Les douleurs de la région précordiale, Le quinzaine therap. **14**:307-312 (Sept. 10) 1912.

the sufferings invariably have subsided. This has led me to believe that a heart too large for its confining limits is able, on account of its constant motion, to exert a sort of chronic traumatism on the surrounding sensory nerves, and become in this way the cause of precordial pains. I hasten to add, however, that this hypothesis might not explain satisfactorily the phenomena whose origin we are just discussing; for many patients with identical valvular lesions, and with a cardiac distention equal or greater, always appeared free from precordial pains. Something else is necessary for the production of such pains."

And finally Esmein decides to appeal to the vague notion of neurotic tendencies, evidently insufficient to overcome the objections that he himself brings forth.

The natural rôle of the musculature of every hollow organ is to react on its contents and make them progress. That progress is subject to chronologic laws, whose fulfilment is a requisite of health. Experimental physiology and clinics have slowly revealed these laws, with the aid of polygraphy and electrocardiography for the circulatory, and with roentgenology and coprology for the gastro-intestinal tract. As soon as an obstacle of any kind opposes the rhythmic or periodic movements necessary for such progress, irregular and more or less violent muscular contractions are produced. If the obstruction is so sudden that it is not checked with equal rapidity by the sympathetic defenses, the somatic ones are aroused, and, by the mechanism proposed above, send the painful impulses to the brain as signals of distress.

This takes place in angina pectoris, where a sudden rise in diastolic pressure, index of peripheral vascular resistance, urges the left ventricle in vain to raise at once the systolic pressure to a convenient level; the paroxysm is controlled, if managed in time, by vasodilatory medication. Likewise in colic of nephritis, hepatic or intestinal origin; also in gastric pains, which, as Leon Meunier [28] believes, are due directly, with the exception of ulcerative lesions, not to disorders of secretion but to the motor delay.

On the other hand Briscoe,[29] admitting that it is quite evident that the overfatigued muscles give rise to referred pain in distant areas, points out that when certain respiratory muscles are sensitive and subjected to pressure the area to which the pain is referred corresponds to those similarly affected in angina pectoris.

And in regard to the abdominal viscera, we must quote Brüning and Gohrbandt's contributions [30] on the pathogenesis of pain in intestinal colic. For these authors "pain is only caused by the mucous

28. Meunier, Léon: Treatise Therapeutique Clinique by A. Martinet, Masson et Cie, 1921, p. 1051.

29. Briscoe, C.: The Origin of the Anginal Syndrome, Lancet **2**:1257 (Dec. 17) 1921.

30. Brüning, F., and Gohrbandt: The Pathogenesis of Pain in Intestinal Colic, Klin. Wchnschr. **58**:1431, 1921; abstr., Nerv. & Ment. Dis., September, 1923.

membrane in animals when the irritation leads to intense muscle contraction. The contraction pain is undoubtedly initiated in the intestinal wall and, by assuming that the pain is caused by the instrumentality of the sympathetic, its special quality is explained. By numerous experiments with oil of mustard it was shown that after stroking or brushing the mucosa, pain results only on strong contraction of the intestinal wall. As soon as muscular spasm develops and until it dies away, there is clear evidence of pain, and unless this motor reflex occurs there is never pain."

Now we can understand this conclusion of Mackenzie [31]:

"The violent stimulation of the spinal cord may leave after its subsidence an irritable focus in the cord rendering the portion of the cord more susceptible to stimulation, so that it becomes easier for future attacks of angina pectoris to be provoked. That irritable focus can be demonstrated to exist in some patients by the hyperalgesic state of the skin and muscles and other subcutaneous tissues in the region where the pain was felt."

MacKenzie also thinks rightly in attributing the crisis of angina pectoris to the diminution of the myocardial power of contractility, and the exhaustion of its reserve energy by overexertion. But it is possible to admit that the persistence of abnormal stimuli of low intensity, as in Esmein's patient, may be able to maintain in the part of the spinal cord which endures these a certain degree of permanent susceptibility which makes that part apt to respond with violence to any new superadded stimulus, incapable of provoking in itself, under ordinary circumstances, real paroxysms.

As Lutembacher [32] well points out:

"There is no relation between the degree of myocardial failure, the gravity of its lesions and the appearance of a painful syndrome. In this way the dilatation of the right side of the heart, which is generally progressive, does not cause pain from the distention. Its insufficiency becomes apparent only from cyanosis, dyspnea, phenomena of stasis. The left side of the heart, on the contrary, is frequently subjected to sudden distention, offering, furthermore, a greater resistance than that of the right, and before it dilates, it distends and causes pain. In the course of aortic lesions of arterial hypertension, the distension manifests itself by dyspnea always accompanied by dull spasmodic pain. The greatest crisis appears when the left ventricle is suddenly overstimulated; and it is then that we observe a painful retrosternal cramp; which by its characteristics, its radiation to the left arm, the accompanying mental anguish and its possible termination in sudden death is entirely similar to angina pectoris."

In rhythmic contractions, the periods of rest alternating regularly with those of activity of the muscular fibers allow the latter to recover

31. Mackenzie, James: Diseases of the Heart (Footnote 2) p. 76.

32. Lutembacher, R.: Douleurs de distention cardiaque. Angine de decubitus, Presse méd. **30**:281 (April 1) 1922.

the biochemical state which restores their contractile power. In this way they obey the chronologic law which governs the function of the organ to which they belong, most probably under the control of the so-called neuromuscular cells, which, as Desfosses [33] quotes, "are found more or less distributed among the nervous elements of the plexuses, not only cardiac but also intestinal, and grouped in certain regions in whose vicinity the tone is increased, the irritability and contractility are greater, and the peristaltic waves are more pronounced." Irregular or atypical contractions on the contrary, exhausting sooner or later the reserve energy, tend toward distention of the organ with evident embarrassment in the normal cycle of its physiologic activity.

The application in each particular case of this generic conception of the mechanism of splanchnogenic symptoms is not only useful for their better understanding, but also for the explanation of certain syndromes of a more complex and diffuse character, as I have already shown elsewhere [34] and as I intend to describe fully in a subsequent work.

238 West One Hundred and Sixth Street.

33. Desfosses, P.: Le système sympathique; son anatomie générale, Presse méd. **29**:543 (July 9) 1921.

34. Arnau, R. Ruiz: Un caso de pseudotétanos, An. méd. de Puerto Rico **1**:238, 239, 240 and 241 (Sept.) 1921; La lymphectasie tropicale primitive, Paris, A. Maloine et fils, 1916, p. 125, 126, 127, 128 and 129.

Obituary

HAROLD NICHOLAS MOYER

1858-1923

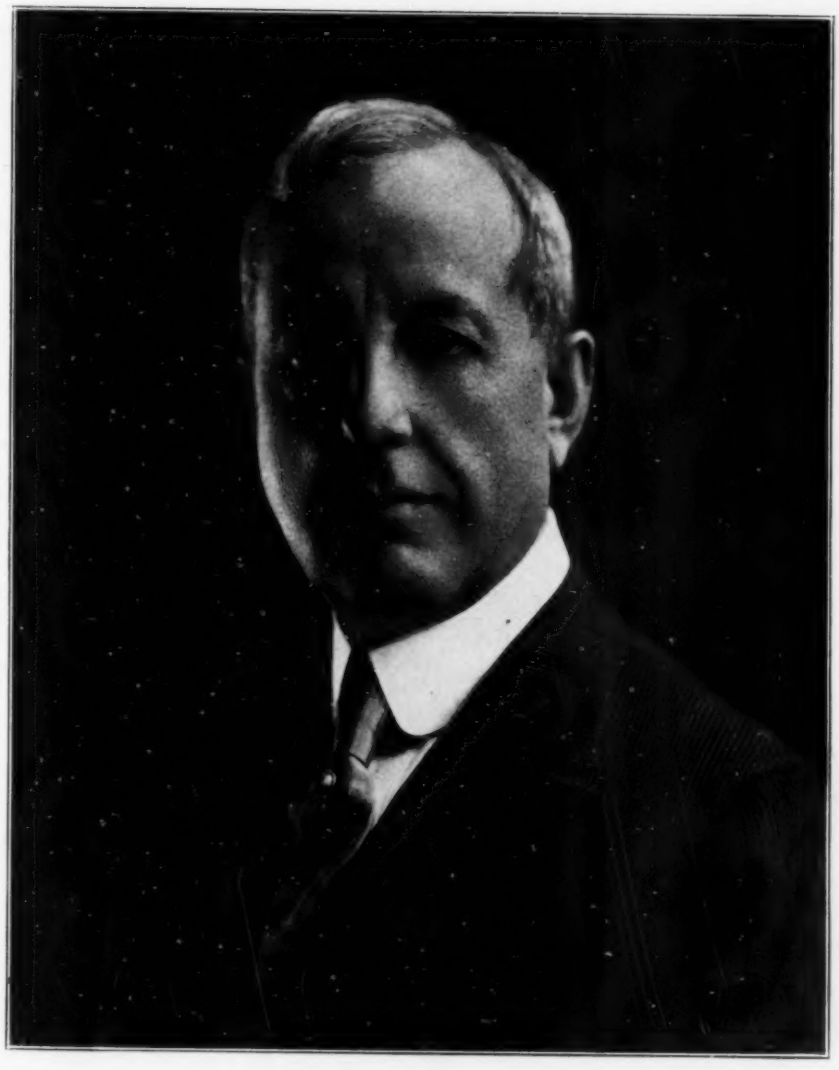
Dr. Moyer was born in Canajoharie, New York, Aug. 14, 1858, and died in Chicago, Dec. 14, 1923.

After finishing the public schools in Chicago, Moyer went to work as a bookkeeper, at the same time taking private instruction in Latin and other branches. He then entered Rush Medical College and graduated in the spring of 1879. Almost immediately he became assistant physician in the Cook County Infirmary, the psychopathic department of which was then officially known as the "Cook County Crazy House." Moyer had charge of the lying-in ward, at that time a busy ward. Early in 1881, he became assistant physician at the Illinois Eastern Hospital for the insane at Kankakee, where he remained for about two years.

Following this service, Dr. Moyer went abroad for eighteen months, working principally at Heidelberg and Berlin.

On his return to Chicago, he opened an office on West Madison Street, in what was probably the busiest, most populous and most cosmopolitan part of the city. And then began for Moyer diversified activities with many people of many kinds. At his alma mater he was appointed in rapid succession lecturer on histology, lecturer on and later professor of physiology, and assistant professor of diseases of the nervous system. Then he became adjunct and later assistant professor of medicine. He was neurologist at the Central Free Dispensary (Rush Medical College) and then chief of the neurologic clinic. He served Rush Medical College for nineteen years. In the meantime, he was also lecturer on and later professor of nervous diseases in the Postgraduate School and professor of nervous and mental diseases in the Chicago Clinical School. He was appointed neurologist to the Cook County Hospital, and for many years held clinics there. For a time he was lecturer on railway medical jurisprudence in the Kent College of Law.

In 1888, he became county physician, a political job which brought him in contact with politicians and men about town; a contact he did not shun, but which never contaminated him. As county physician he had charge of the "detention hospital" for the insane, now the psychopathic hospital. Moyer never lost his interest in this institution and its inmates, and at the time of his death had been chief of the visiting staff for ten years. He had been on the medical staff of St. Luke's, Columbus, Mercy and other hospitals.



HAROLD NICHOLAS MOYER

1858-1923

Early in his career Moyer became interested and active in medicolegal matters. His temperament and tastes, his aptitude and training combined to make him effective and successful in this work, so that in less than ten years after his return from Europe he was the best and probably the best known medicolegal expert in Chicago. With the years this work grew at the expense of his other practice, and for some time prior to his death constituted the major part of his occupation. Of late his function had been largely that of advisor to large corporations; he seldom appeared on the witness stand. As he had acquired an extensive knowledge of law and a wide experience of courts and juries, besides possessing an acute mind and a judicial temperament, he was an invaluable consultant in medicolegal cases.

While from the time of his service at Kankakee Dr. Moyer was known more or less as a psychiatrist and neurologist, he started as a general practitioner, accepting all work which a young physician could obtain. And he had his full share, acquiring a good general practice, and before long a good consultation practice. Although known more and more as a neurologist and psychiatrist, Dr. Moyer never lost interest in the problems and practice of general medicine. Indeed, a few years ago he began to write a textbook on the practice of medicine, but never finished it.

Moyer began to write early. He wrote much and he wrote well. Considering that he was not a college man, did not even graduate from high school, he wrote astonishingly well. His style was simple, direct and lucid. The Crerar Library lists one hundred and ten papers covering a wide range of topics. Most, of course, relate to neurology, psychiatry and forensic medicine, but he also wrote on injury from electric currents, boric acid in leukorrhea, hematuria, poisoning with Paris green and with colchicum, pulmonary edema, hypodermic use of arsenic, catarrhal gastritis, skotography ("Prof. Roentgen's discovery"), state supervision of the tuberculous, hot air treatment of nervous and joint affections, the medical editor and original communications, circumcision and syphilis, incidence of nervous diseases in life insurance examinations, medical graft, biographical papers and on other equally diverse topics. From 1891 to 1894, he averaged more than six papers a year.

For twelve years he was the editor of *Medicine*, an excellent monthly journal, in 1907 absorbed by the *Therapeutic Gazette*. His editorials invariably were brief and clear; sometimes trenchant; instructive, interesting or amusing, always readable.

In addition to the foregoing literary output we might add sundry open correspondence in medical journals, addresses to lay gatherings and after-dinner speeches, not to mention political speeches which were

an occasional diversion of his earlier years. The last paper Moyer wrote, only a few weeks before his death, was an excellent one on dreams, read before the Chicago Literary Club.

In 1905, the degree of LL.D. was conferred on him by Notre Dame University.

Perhaps because of his legal knowledge and connections, Moyer was at different times active and most useful in framing and passing the various medical practice acts of Illinois as well as in defeating such vicious bills as are constantly coming before our legislative bodies, and in influencing legislation regarding expert witnesses. For many years he was chairman of the medicolegal committee of the Illinois State Medical Society and for a time served the Chicago Medical Society in the same capacity. Certainly no one in the state, physician or lawyer, had so well in hand the matter of medical liablity and malpractice. An attorney who specializes in this field said, "He was better than all the lawyers you could get." In preparation of the case, knowledge of the law and of the ways of judges and juries, and in judgment of the theory on which a case should be tried, he was without a peer. His services to the profession in such matters can never be estimated, and yet they were entirely gratis, given modestly and cheerfully.

But let it not be imagined that he simply lent his talents to defend physicians under all circumstances. For the deliberate offender he had no sympathy. To one accused of abortion he was overheard to say, "No sir. You are guilty; guilty as hell, and don't imagine that I shall do anything to help you."

At the time of his death Moyer was a member of twelve medical societies and had read papers before all but one. He had been president of the Mississippi Valley Medical Association, the Illinois State Medical Society, the Chicago Medical Society and the Chicago Neurological Society (twice). On the floor he held the attention of the audience because he never rose unless he had something to say, always spoke clearly and to the point and knew when to sit down. He was just as successful as a listener because he was keenly appreciative of excellence in others, his interests were catholic, and he loved good work. But especially here as everywhere was he full of kindliness and good fellowship and alive to the humorous.

That is an outline of what Moyer did. What of the man himself? What he was overshadowed what he did. Perhaps his most outstanding qualities were probity and generosity. With them we must place geniality. Of brains, he had plenty, but his most precious gift was his disposition. I am sure he would rather have been a good fellow than a good physician. In truth he was both, but the former contributed more to his happiness than the latter, and infinitely more to the happiness of

his friends. Once in speaking of a talented colleague, Moyer said to me in a tone of pathetic regret, "He isn't a bit of a good fellow, is he?" In his estimation that was a real calamity.

His generosity was all-embracing. Not only the generosity of giving freely of his time, his talents and his money, but the generosity that can see the good in the presence of bad and accord to every one his full share of credit. He showed abundantly of kindliness, and he reaped a plenteous harvest of friendship. I think I have known no man with so many friends of so many kinds. Physicians, lawyers, clergymen, business men, laboring men, politicians; employers and servants; the aristocracy of wealth, the pauper on the county; the social élite and the social outcast; the cream of the educated and cultured and the dregs of the submerged tenth; all found something in Moyer that they liked. Because they all had some appeal for him.

But he was no indiscriminating admirer. His mental caliber was too great for that. And he was frank with his friends. In the early days of our friendship, Moyer heard the first paper I ever read before the Illinois State Medical Society. As we were walking back to our caravansary, he said, "P., that paper of yours seemed to take mighty well, but I can't see that there was much in it." And he was right. But his criticism obviously was made in such a kindly spirit that it was like a pat on the back.

Moyer never took himself too seriously, and assuredly he enjoyed a joke on himself better than on another, but his tendency to persiflage apparently was congenital and incurable. In the earlier years of his teaching, his chief cautioned him against assuming such a light vein in his clinics; he said the students would misconstrue it and underestimate him. "But of course," Moyer told me years later, "I couldn't help it." The following from an address on disturbances of the fifth nerve before the Chicago Dental Society is fairly typical:

"I may mention that among my credentials is that I am known as the castor oil doctor. That term has been applied because I have used castor oil in the treatment of trifacial neuralgia with a degree of enthusiasm and persistence worthy of a better cause; not that I want to take full credit for the castor oil treatment. I was a disciple rather than a leader in that great movement."

From the foregoing one may readily guess that Moyer was the most companionable of men. In any gathering he was a treasure trove. He could be hilariously jovial or cosily chatty; a raconteur of parts, he was a most sympathetic listener. He was fond of good food, good drink and good company, but equally fond of intellectual accomplishment and high ideals.

H. T. P.

Abstracts from Current Literature

Relation of Puberty to Behavior and Personality in Patients with Dementia Praecox. Charles E. Gibbs, Am. J. Psychiat. **3**:121 (July) 1923.

From a survey of the personality of nine individuals who subsequently became psychotic, Gibbs sought to answer tentatively the following questions: When and where does the individual get his peculiar personality? When does personality leave off and psychosis begin? Six of the patients were diagnosed dementia praecox, one manic-depressive, one psychosis with psychopathic personality, and one "emotional, paranoid episode." In every instance there was a definite change of makeup at puberty which practically amounted to a complete reversal of dispositional traits. The source of personality, or in other words the factors that go toward its shaping and differentiation, are to be sought in the reaction which is chiefly accomplished at puberty when "external, environmental, and psychologic" elements, matters of experience in general come into contact with "internal, physiologic, constitutional, and hereditary factors." In this connection it is of practical value to note that in Gibbs' patients the reversal of personal characteristics at adolescence was frequently accompanied by more or less profound metabolic disturbances. The author's discussion concerning the relation of puberty to psychopathic behavior deserves to be quoted, particularly in view of the inferences which are more or less applicable to the present status of the problem of schizophrenia. "The essential and fundamental changes of puberty are biologic and the behavior changes which characterize the psychopathic personality relate to emotional and instinctive factors. There is considerable evidence to indicate that these biologic processes of growth and metabolism must carry the organism on to physical and functional perfection and maturity before maturity and socialization of emotional and instinctive behavior can be attained. It seems quite possible that the biologic changes awaken and activate the more or less dormant reproductive instinct and the emotions which drive it, the instinctive and social behavior reactions being thereby conditioned and new ones formed. Abnormalities in the biologic factor would then be expected to be reflected in the behavior. Since the biologic changes involve the gonads and the behavior changes involve the instinct of reproduction, it seems no wonder that their manifestation should be in reference to sex and give a sex coloring to the clinical picture of the psychosis in so many cases.

"These biologic processes probably involve, not only the gonads, but even more essential and more fundamental processes of metabolism which go on before puberty and which are essential to physiologic puberty. As has been pointed out elsewhere, other glands and other functions are essential to physiologic puberty as well as the gonads, and the psychologic inadequacy shown by some of these individuals seems to be a total one involving the whole organism rather than specifically gonadal. The existence of psychopathic traits before puberty in certain cases indicates the 'reaching back into childhood' of these biologic inadequacies."

In regard to the second query the author concludes that "in certain cases of dementia praecox it is difficult to determine whether seclusive behavior appearing at puberty is a part of the personality or a part of the psychosis."

It is not altogether clear whether Gibbs selected his patients having in mind certain personality requisites or not. If selected, much of the force of the argument is lost. In any event the series is too small to justify final opinions. However, the suggestions arising from Gibbs' work constitute a timely contribution and should stimulate further intensive studies and elaboration.

STRECKER, Philadelphia.

THE PATHOGENESIS OF LANDRY'S PARALYSIS. E. A. GRÜNEWALD, J. f. Psychol. u. Neurol. **29**:403 (March) 1923.

Grünewald reports the case of a neuropathic, single woman, aged 26, who had for years been subject to attacks of intestinal colic with obstinate constipation. On the seventh day after the onset of one of these attacks she developed a flaccid paralysis involving first the lower extremities, then the upper and at the end of three weeks the cranial nerves and the respiratory center. The involved muscles showed partial reaction of degeneration and a partial quantitative deviation resembling the myasthenic reaction. Objectively there were no evidences of radicular or peripheral sensory involvement. There were, however, transitory subjective sensory disturbances of the nature of hypesthesias and paresthesias. Associated with the slowly progressing ascending paralysis the following disturbances of the vegetative nervous system were noted: intestinal spasms, gastrosuccorrhea, galactorrhea, excessive salivation and epiphora. Throughout the entire illness there were also present: porphyrinuria, oliguria and obstinate constipation. On the twenty-second day of the disease there developed bulbar symptoms with attacks of dyspnea; the dyspnea could be controlled, for a week, by the administration of lobelin, but the intestinal spasms could not be influenced by medication. The cerebrospinal fluid was negative bacteriologically; the blood Wassermann reaction was negative; there was nothing unusual about the blood picture. The disease lasted six weeks and death was due to respiratory paralysis.

A study of this and similar cases reported in the literature leads the author to believe that pathogenetically Landry's paralysis cannot be regarded as a disease sui generis. He is rather inclined to look on it as a biologic manifestation of various pathologic processes—a syndrome induced by the action of a toxin or toxins on an allergically (in the sense of toxin-oversusceptibility) reacting nervous system. In the case reported it is assumed that the endotoxin of porphyrin had a neurotropic effect on the nervous system. This assumption is largely based on Günther's studies of hematoporphyrins. Günther has found that there exist a large number of clinical cases of chronic porphyrinuria in individuals with an anomalous constitutional make-up, in whom there occurs an increased formation and diminished excretion of hematoporhyrin. The latter is then deposited in the tissues and under photodynamic influences gives rise to various dermatologic manifestations (pigmentation, etc.). These same individuals are subject to attacks of acute porphyrinuria, which is characterized by the symptom triad of intestinal colic, vomiting and obstinate constipation with the appearance of porphyrins in the urine and feces. When these attacks become unusually frequent there may develop complications on the part of the nervous system ranging from the milder forms of polyneuritis to the fatal forms of Landry's paralysis.

These cases are best explained as follows: Certain individuals are subject to periodic attacks of disturbances of metabolism. These metabolic crises are of great significance as a source of toxins for the entire organism. The effect

of this general toxemia is manifested by excretion of metabolic products of disease as well as by disturbances on the part of the vegetative and motor nervous systems. Such metabolic disturbances may arise autochthonously (porphyrins), or they may be due to exogenous noxae, such as the chronic abuse of sulphonmethane, barbital and morphin, chronic lead poisoning, typhus, infections, etc. Snapper has reported three cases of porphyrin colic, in two of which fatal Landry's paralysis developed. This author believes that in porphyrin colic repeated metabolic disturbances occur and give rise to certain toxic products which first produce degenerative processes in the retroperitoneal nervous structures and later affect the remaining parts of the nervous system. In most of these cases, however, if not in all, it seems that there must exist a predisposing constitutional anomaly which renders the organism labile and readily susceptible to the exciting cause—the toxin.

Grünewald also points out the parallelism between other toxins, especially that of diphtheria, and the hypothetical toxin of Landry's paralysis. Both of these toxins seem to have a paralyzing effect; they both attack lipoids, and preferably the phosphorus and nitrogen containing phosphatids rather than the cholesterin group. The effect of the toxin on the colloidal chemistry of the cells seems to be the same in both diseases. Clinically the dynamic effects of the regressive changes of the cell protoplasm find expression in both of these diseases in paralysis, and in both of them the motor tracts are the first to show the injurious effects of the toxin. The greater vulnerability of the motor components of the nervous system to these toxins is attributed to the fact that in the organism as a whole these physiologic units are subjected to unusual functional stress, and therefore, play a very important rôle in metabolism—assimilation and dissimilation. Biologically then, the protoplasm of the motor neuron is, par excellence, unusually exposed to the effects of the products of decomposition.

The intimate association of motor nerve symptoms with those of the vegetative nervous system (galactorrhea, gastrosuccorrhea, etc.) in Landry's paralysis has led many authors to regard this disease as a system disease, in which the pathologic process affects two distinct systems, motor and vegetative. The ready participation of the latter is attributed to certain morphologic factors. Indeed, the simultaneous involvement of both of these systems in Landry's paralysis has led Walter to attach great pathogenetic significance to its causation, especially so because the primary seat of the disease is in the anterior root—a root neuritis. Inasmuch as the radix anterior anastomosis in the anterior roots with the rami communicantes which unite the lateral columns of the cord with the ganglia of the sympathetic limiting zone and with the sympathetic nerves, Walter believes it is within the anterior nerve root that the poison affects by continuity the sympathetic component as well as the motor component of the root.

KESCHNER, New York City.

PSYCHOTIC SYMPTOMS OF EPILEPSY. HARLAN L. PAINE, Am. J. Psychiat. **2**:713 (April) 1923.

Paine studied fifty-three epileptics, particularly from the standpoint of their psychotic symptoms. He makes out a somewhat better case for the victims of "falling sickness" than is usual, and only 42 per cent. of his patients approached the "typical epileptic disposition" vividly described by Bianchi: "The whole life of the epileptic shows hatred. It bursts forth in all its brutality on the slightest provocation; the horrid, the brutal and all that is evil, destruction and death are present in his mind." The dispositional anomalies emphasized

by De Fursac, namely: irritability and variability of moods; egoism; duplicity; apathy; sudden impulsive reactions, violent at times; terrific fits of anger; lack of consistency between conduct and ideas; more rarely, abnormal stubbornness and tenacity, were present in less than half the patients. Hyper-religiosity appeared only four times in the series. Psychotic episodes, varying from extreme irritability to violence and frequent confusion, were displayed by thirteen patients before the convulsion and in thirty-three they were postconvulsive. Twelve patients had a history of epilepsy in the direct ancestry. One patient committed suicide and in this connection it is interesting to note that self-destruction is extremely rare, there having been only two instances during a period of twenty-four years at the Monson Epileptic Hospital.

STRECKER, Philadelphia.

HISTOLOGIC LOCALIZATION IN THE FOREBRAIN OF REPTILES. MAXIMILIAN ROSE, J. f. Psychol. u. Neurol. **29**:219 (March) 1923.

The object of this investigation was to determine the structure of homologous elements in the cerebral cortex of the lower vertebrates in order to establish a basis for the comparative histologic topography of the cerebral cortex of all vertebrates. A similar investigation had previously been undertaken in birds and its results published by the same author in the *Journal für Psychologie und Neurologie*, 1914. In both of these investigations the cortex as well as the corpus striatum was studied from the point of view of anatomic localization. Owing to the difficulty of obtaining animals, the author had to limit his investigation to the study of only the most important representatives of individual species of reptiles. He selected the following animals: Crocodilia: *Alligator lucius, Crocodilus palustris;* Chelonia: *Emys lutaria, Testudo graeca;* Lacertilia: *Varanus bengalensis, Lacerta viridis, Lacerta agilis, Lacerta muralis, Anguis fragilis, Chamaeleon;* Ophidia: *Tropidonotus natrix, Boa constrictor.* Frontal horizontal and sagittal sections of the brain were studied. The brain was first embedded in paraffin, after which sections 18 microns thick were made, and stained with cresyl violet according to the Bielschowsky method. The sections were then photomicrographed in magnifications of 30 and 180 diameters.

From his work on the brains of birds the author found that a topographic study based on the structural characteristics of the cell yielded better results than one based on a study of myelinated fibers. This he also found to be true in the case of reptiles, and, therefore, he devoted himself chiefly to the study of cytoarchitecture, employing fiber preparations only for purposes of comparison. With this view in mind he paid special attention to: (1) form of the cell; (2) size of the cell; (3) inner structure of the cell; (4) quantitative relationship between the pyramidal cells, granules, and other varieties of cells; (5) the closeness with which the cells are packed together; (6) the intensity with which they take up stains; (7) special forms of cells; (8) the width of the cortex; (9) the width of the individual layers of the cortex and (10) the number of layers.

In none of the birds and reptiles studied could the author find in the forebrain any evidences of an isogenetic cortex. The cortex was throughout allogenetic (allocortex). The isogenetic cortex, therefore, represents the highest degree of cortical development, and is found only in mammals. According to his views the most important definite morphologic characteristic of the isogenetic (neopallial) cortex is one consisting of seven layers. No such cortex was found in any of the animals examined. As a matter of fact, some of the

lower vertebrates at times presented great difficulties in the attempt to determine which part of the cortex was allocortex and which corpus striatum. Both of these structures develop from the same anlage—telencephalon. Embryologically the striatum is a sort of "aborted" cortex—a cortex which, after a certain period, ceased to develop further; it lacks the most important criterion of a distinct cortical layer, namely stratification.

The following types of cortex were examined histologically in each species under investigation: area praepyriformis bulbaris, area praepyriformis communis, tuberculum olfactorium, formatio Ammonis, nucleus amygdalae, septum pellucidum and the bulbus olfactorius. In addition to these the following histologic centers of the corpus striatum were studied: hyperstriatum, mesostriatum, ectostriatum and the nucleus entopeduncularis. The olfactory tubercle was found to be well developed in all reptiles, but its structure varied greatly in the different species. In crocodiles and cheloniae it was identical with that of small mammals and birds. In *Varanus* the ventricle is not situated in the center of the bulb as in mammals, birds, crocodiles and cheloniae, but it surrounds in a cleft-like fashion the entire bulb except its mesial portion. This leads to the formation of a dorsal, lateral and ventral ventricular wall. The lateral wall is the widest, but becomes constricted as it approaches the dorsal and ventral direction. The main portion of the bulbus consists therefore of the thickened mesial ventricular wall. It is here that the greatest number of the olfactory glomerules with the olfactory fibers leading to them are found. The glomerules are situated deeply within the bulb, forming its chief bulk; they are surrounded by other layers of the olfactory bulb under which the pyramidal layer comes into view with unusual prominence. The smaller lacertilia and ophidia occupy in this respect an intermediate position because in these the frontal portion of the bulbus resembles structurally that of the crocodile and cheloniae, while its caudal portion resembles that of the *Varanus*.

The architectural plan of the corpus striatum is the same in reptiles (except in the cheloniae) as in birds, except that in the former it shows less differentiation, as a result of which it contains a smaller number of histologic centers. This, however, is not the case with the cortex. The latter, while it is true that it resembles the cortex of birds, i. e. it is throughout allogenetic, its differentiation both as regards inner structure as well as the number of histologic centers is far in excess of that in birds, and approximates rather the mammalian cortex. It would seem, therefore, that in reptiles the cerebral development is at the expense of the corpus striatum and in favor of the cortex itself. This is probably the reason that in reptiles most of the histololgic centers of the mammalian allogenetic cortex are so well developed at the same time that so many of the histologic centers of the corpus striatum are so poorly developed. Apparently the brains of reptiles show the same developmental tendencies as those of mammals, i. e., greater development of the cortex itself with a simultaneous defective development of the corpus striatum.

KESCHNER, New York City.

KIDNEY MALFORMATIONS IN THE MENTALLY DISORDERED WITH REPORT OF A CASE OF CONGENITAL CYSTIC KIDNEYS AND LIVER. NOLAN D. C. LEWIS, Am. J. Psychiat. **3**:65 (July) 1923.

Lewis is led to believe from his necropsy material that congenital abnormalities and arrests in kidney development, such as entire absence of one kidney or extreme atrophy, large solitary cyst, lobulations, multiple ureters, and

vessel peculiarities are of more common occurrence in the insane than in the mentally normal. For instance, an unpaired kidney was found five times in 4,500 necropsies as contrasted to its reported average occurrence of but once in 4,000 individuals who were not mentally diseased. Morris at Middlesex Hospital, London, discovered five kidneys with large single cysts in 2,610 necropsies; and the author, two in 500 postmortem examinations. The rarity of this condition may be inferred from the fact that a search of the literature revealed only 100 cases. Lewis suggests a correlation between his findings and the frequency of kidney anomalies in the lower, more primitive races of men, but does not support the assumption by any statistical data.

STRECKER, Philadelphia.

TREMOR IN CEREBELLAR DISEASE. F. LEIRI, J. f. Psychol. u. Neurol. **29**:429 (March) 1923.

Leiri could find in the literature but two other cases resembling the one which is the subject of this paper. This is not surprising when one considers the comparative rarity of cerebellar vascular lesions. His patient, an arteriosclerotic, aged 70 years, during the last few years of his life showed an intention tremor confined to the right side of the body and involving chiefly the extremities. Necropsy revealed, in addition to an état lacunaire involving all parts of the cerebrum, pons and both thalami, a softening of the right cerebellar hemisphere with degeneration of the nucleus dentatus and the surrounding substance of the cerebellum. The nuclei fastigii were intact, but there was softening of the nuclei emboliformi and the nuclei globosi on the right side with secondary degeneration in the right brachium conjunctivum. These degenerated tracts could be traced to the nucleus ruber and thalamus on the left side. There was also marked degeneration in the right brachium ad pontem and in the left inferior olive and in the olivocerebellar tracts in the medulla.

The author assumes that the right sided cerebellar lesion gave rise to the intention tremor which involved chiefly the homolateral extremities. Although tremor in cerebellar disease has been frequently described in man, it can nevertheless not be regarded as a common symptom. In experimental cerebellar extirpation in dogs no disorder of motility akin to tremor in the extremities has been observed. In monkeys, however, a lesion so induced gives rise to definite intention tremor of the extremities. Both experimental and clinical evidence furnish abundant proof that there is a great difference in the movements of the extremities in the different species of mammals. In the dog these movements have a relatively poor representation in the cerebral cortex, whereas in the monkey and in man they are to a great extent dependent on the cortex. The movements of the head, on the other hand, are in all the higher mammals closely associated with the cortical centers. This is in harmony with the fact that in the dog the extrapyramidal system is better developed than the pyramidal, while in man the reverse is true, and in the monkey the two tracts are developed to the same degree. The different kinds of movements, then, depend greatly on the varying influences that the cortex exerts during the execution of each particular movement. The principal movements (locomotion and prehensile movements—Munk) are more or less stereotyped and may be regarded as finished complex reflexes. Conditions, however, are different in the case of purposeful or intentional movements; in these the various components of movement are continuously altered by cortical impulses.

To understand the significance of disorders of movements, it is important to bear in mind that during a movement of any part of the body, not only the agonists but also the antagonists are put into activity. After experimental cerebellar lesions in dogs there occurs definite failure of reflex innervation of the antagonists during the movements of the extremities, and, inasmuch as these are "principal" movements, a correction of these defective movements by the cerebral cortex does not occur. The same is also true in the case of head movements (following cerebellar lesions), in which the hypermetria is due to the fact that during them the antagonists fail to functionate. Now, inasmuch as head movements in the dog and in the other higher mammals are definite cortically represented intention movements that may at any moment be corrected by cortical impulses, it stands to reason that every new hypermetric movement in the opposite direction must again be corrected. These repeated corrections give rise to a "pendulum" movement which must be maintained in order that the animal may be able to retain its center of gravity, i. e., it gives rise to a tremor. It is precisely to these attempts at cortical correction of the hypermetric movements of the head after experimentally induced cerebellar lesions that one must look for an explanation of the causation of the intention tremor in cerebellar disease.

As to localization, Leiri points out that the dentate nucleus is the point of origin of the brachium conjunctivum and most of the efferent pathways; it is also the point of convergence of numerous centrad conducting paths. Bárány, Ferrier and Turner, Fabritius, as well as Leiri, have shown that lesions involving this region are especially prone to give rise to intention tremor on the side of the lesion. In the case reported there was no head tremor. This, Leiri believes, can be attributed to the fact that microscopically both nuclei fastigii were found to be intact, and he ventures the hypothesis that these nuclei are concerned with head movements, while the dentate nuclei are concerned with movements of the extremities.

KESCHNER, New York City.

THE DEVELOPMENT OF THE TELENCEPHALON IN SPHENODON PUNCTATUM. MARION HINES, J. Comp. Neurol. **35**:483, 1923.

The forebrain vesicle of this interesting reptile can be divided into Herrick's four quadrants. In the dorsomedial quadrant of the wall of the developing hemisphere the primitive hippocampus may be identified. The ventromedial quadrant, the septum, develops similarly to that of man. Within the dorsolateral quadrant, between the pyriform lobe ventrally and the hippocampus medially lies a region which contains several cortical layers. This small area represents all of the neopallium or general cortex that this animal possesses. The ventrolateral quadrant, while following the same course of development as in man, is of especial interest in *Sphenodon*. This area is separated from the neopallium above by a ventricular sulcus and from the septum below by the angle of the ventricle. Two ridges project from its medial wall into the ventricle: a dorsal or neostriatal ridge and a ventral or paleostriatal ridge. The latter is only slightly differentiated. The anterior part of the neostriatal ridge is homologous with the lateral part of the nucleus caudatus and a part of the putamen in man. This part is the neostriatum proper and is connected with the thalamus. The remainder of the neostriatal ridge is the archistriatum or that portion whose connections are predominately olfactory. Within the archistriatum a definite nucleus can be recognized, the nucleus ventromedialis, which is homologous with the amygdaloid complex. The portion of the

archistriatum exclusive of the nucleus ventromedialis is connected with the base of the olfactory bulb. This separation of the archistriatum into two components is significant because the amygdaloid complex is characteristic of amphibia while the olfactoneostriatal system appears for the first time in phylogeny in reptiles.

GRAY, Chicago.

THE RELATION OF THE BRODMANN-VOGT AREAS TO THE CEREBRAL CONVOLUTIONS. G. WETZEL, J. f. Psychol. u. Neurol. **29**:434 (March) 1923.

Brodmann and Vogt have shown that there is a causal connection between the development of the cerebral fissures and that of the architectonic cortical areas. These observers also insist on the necessity of distinguishing between the value of the fissures for the architectonic orientation of the cortex and the significance of the architectonic areas as regards the origin of the fissures. In this communication Wetzel supports the above authors' views and in addition points out that there is a definite developmental relationship between these areas and the fissures, and that this relationship is not haphazard but follows certain definite laws. He believes that the special arrangement of the cerebral fissures depends on the peculiar conformation of the different cortical areas, and represents a special form of development and differentiation, i. e., the general surface of the entire brain and of each lobe is subject to local modifications, which depend on the direction of the fissures and their intensity of development. The direction and course of each fissure and gyrus is actually determined by the areas, and their histologic differentiation is to a large extent instrumental in bringing about their growth and development.

From an embryologic point of view it appears that the fissures make their appearance much earlier than the areas, i. e., the fissura calcarina and Rolando appear before the differentiation of the area striata and area gigantopyramidalis has taken place. Wetzel believes that the definite determinant regions on the particular biologic condition of which the growth and differentiation of the convolutions is largely dependent, exist from the very beginning of cerebral development. The location and differentiation of the areas are not founded on any basis of mechanical development, although their relation to the fissures seems to depend on some such mechanical basis.

Wetzel confirms Vogt and Brodmann's views that the histologic differentiation of the areas and their multiplicity must be looked on as equivalents of the degree of development. According to him, areas developed in a different way must also give rise to alterations in the course and development of the corresponding gyri. The richer development of the areas in man as compared with that of monkeys is parallel with the unusually rich development of the convolutions in the former. Apparently these areas are of great significance from points of view other than those of topography.

KESCHNER, New York City.

SOME RESULTS OF NERVE ANASTOMOSIS. SIR CHARLES BALLANCE, Brit. J. Surg. **11**:327 (Oct.) 1923.

The author presents the results of the lateral implantation of the two ends of a divided nerve into a neigboring, uninjured nerve, and shows that this method has been attended with gratifying results. There is nerve regeneration when the distance between the two ends of the damaged nerve is too great to permit them to be sutured. He advocates the use of finest iron-dyed arterial

silk and a fine straight needle (Van Horn). One or two sutures only are required and these may be placed without special regard for the perineurium. He does not advocate the use of Cargile membrane and, indeed, feels that any tissue, especially from autogenous living grafts, is often very unsatisfactory. The nerve ends should be freshened with a sharp knife and not with a dull instrument or scissors.

Ballance believes that end to end anastomosis is the method of choice, but, in cases in which large areas of the nerve have been disturbed, double lateral implantation into an adjoining nerve may bring wonderful results. He cites three experiments on monkeys in which the median, musculospiral and popliteal nerve ends were implanted from 3 to 6 mm. apart. In each of the three monkeys, great return of function was noted in the distribution of the cut nerve.

During the war, a similar operation was performed on wounded soldiers in whom large portions of nerve had been destroyed. Double lateral implantation was effected in one case of loss of the external popliteal nerve, the two stumps being implanted into the internal popliteal. In another case the musculospiral was implanted in two places into the median in the forearm; in still another the median was implanted in two places into the ulnar; and also the ulnar nerve of the forearm was implanted in two places into the median. Ballance was unable to follow the results of these cases owing to his absence from England for some years.

The author holds the view expressed by Durante that the peripheral nerve is laid down as a chain of cells, and that within the protoplasm of each cell are developed the myelin sheath and axis cylinder. He adds that those who hold this view will have no difficulty in understanding the success of the operation of double lateral implantation.

The following cases are presented:

1. The posterior cord of the brachial plexus was implanted in two places into the side of the outer cord. No other operation was possible. Six years after the operation, the forearm and hand were much wasted, but all muscles reacted voluntarily except the extensor longus pollicis and extensor longus digitorium. Continued improvement is expected with further treatment.

2. The median nerve in the forearm was implanted in two places, 5½ inches (14 cm.) apart, into the side of the ulnar nerve. Motor return of function became practically complete in all muscles supplied by the median, as shown in the accompanying illustration. Slight sensory disturbances remained at the ends of the index and middle fingers.

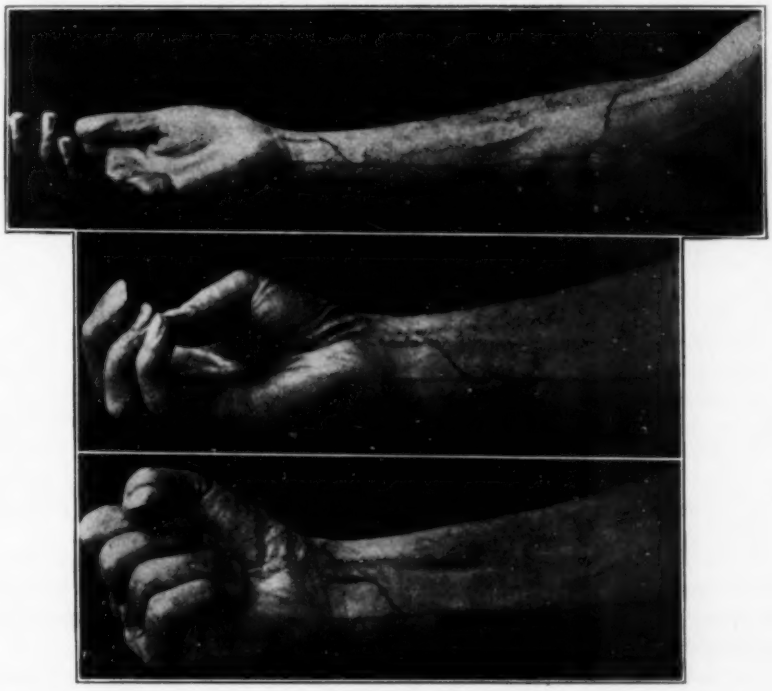
3. The ulnar nerve in the forearm was implanted in two places, 3½ inches (9 cm.) apart, into the side of the median nerve. There was complete return of motor and sensory function in the distribution of the ulnar and median nerves.

4. End to end anastomosis of the ulnar nerve was made 2 inches (5 cm.) above the wrist. The faradic response was obtained in all muscles ten months after the operation. Sensation was normal. The hands retained the appearance of ulnar palsy though they were improving.

Ballance cites the work of Sachs and Malone, in a patient operated on in 1918, who found that a double lateral implantation resulted in complete recovery of function. Experiments by these authors showed that nothing more than a lateral slit in the nerve sheath with a fixation of the implanted end was necessary to obtain even the best results. Any attempt to shape the nerve so as to receive the implant, they found caused unnecessary damage to the nerve used for bridging the gap.

Mr. Joyce's work is also noted by the author and he quotes the results in five of his cases in which this method of implantation was adopted. The results were gratifying in almost every case.

The evolution of the operation for the cure of facial palsy is summarized and a study is made of the various results from different nerve sutures, involving the spinalis, the hypoglossal, and the combined hypoglossal and descendens noni anastomosis, the latter being used to take care of the cut end of the hypoglossal so as to prevent complete atrophy of the tongue on the side of the lesion. The hypoglossal stump was sewed end to end to the facial. He advocates cutting the descendens noni for anastomosis with the facial in the upper part of its course.



Photographs to show the present condition of the forearm and hand in Case 2. The black lines in the forearms show approximately the operation performed: double lateral implantation of the median nerve into the ulnar nerve.

The latest operation he cites is a double anastomosis of the facial to the descendens noni and the communicans noni whose spinal origin is in the first to third cervical nerves.

The author presents experimental work on monkeys showing the results of anastomosis of the divided recurrent laryngeal nerves with the descendens noni, and with the vagus. His results were shown to the members attending the International Society of Surgery July 19, 1923, and at this time, returning functions of the vocal cords were noted. He cites the work of Dr. Frazier, who has performed the operation twice within the past year on the human subject,

with one case showing evident improvement. The results of the operations have recently been presented before the Academy of Surgery in Philadelphia, at its October meeting.

An exercise to assist the return of functions of the vocal cords following this operation is suggested by the author who advocates that the breath be held, then followed by a strong inspiratory impulse causing a movement apart of the cords with abduction of the previously immobile cord as a means of reeducation. Daily practice of this procedure should bring results.

TEMPLE FAY, Philadelphia.

CHANGES IN THE EPISOMATIC MUSCULATURE OF THE VERTEBRATES. HENRI V. VALLOIS, Arch. de morphol. gén. et expér. Monograph 13, Paris, 1922.

This lengthy monograph discusses in great detail the changes which have taken place in the dorsal axial or episomatic musculature of vertebrates. "In all vertebrates except cyclostomes the musculature of the trunk is divided into two parts: one dorsal, the episomatic part; the other ventral, the hyposomatic part. This division, which appears at very early embryonic stages, must be considered fundamental." These two divisions lie laterally in fish, that is to say, the vertebral column is not beneath the dorsal musculature but lateral to it. As development proceeds and limbs appear, their musculature gradually extends dorsad over the dorsal musculature of the axis and covers it to a great extent. In spite of this, it is always easy to distinguish the dorsal musculature (episomatic) from the ventral (hyposomatic) since the "former is supplied by the dorsal branches of the spinal nerves while the latter is supplied by their ventral branches."

After an historical chapter, Vallois discusses in detail the episomatic (dorsal axial) musculature of fish, amphibia, reptiles, birds and mammals.

In fish the episomatic musculature extends from the head to the tail. It is superficially placed. It is limited medially by the dorsal septum and laterally (i. e. separated from the hyposomatic musculature) by the horizontal septum.

The movement in fish is from head to tail. The lateral flexion is due to successive contractions of myomeres. The insertion of these is not on the vertebral column, but on the more caudad myomere by means of a myoseptum. Thus the vertebral column acts as a spring which counteracts this flexing movement rather than as a point of origin and insertion of muscles as in tetrapods, where it aids muscular action.

In land animals, the episomatic muscles begin to pass dorsad and become relatively less voluminous. The limbs, of hyposomatic origin, become more and more important. Further, the hyposomatic muscles assume the function of fixing the pectoral and pelvic girdles and so increase in relative importance.

In urodeles this change is relatively slight as these animals use their limbs to but a limited extent. The episomatic muscles begin to insert on the vertebral, and the vertebral column begins to assume a supporting function rather than one of a spring; in brief, it begins to aid rather than counteract the action of axial muscles. Though urodeles possess no neck some differentiation of the anterior musculature appears.

These three changes in primitive land animals: (1) diminution in relative volume of episomatic musculature as compared to hyposomatic musculature; (2) attachment of muscles to the vertebral, and (3) differentiation of the anterior end of the episomatic muscles (primitive neck muscles) indicate the passage from the sea to the land.

In reptiles the episomatic musculature becomes still less conspicuous, though as compared to birds and mammals it is still very conspicuous. Reptiles require much lateral movement in progression. When such movement is very conspicuous the musculature is the same; while in chameleons, which have very little lateral movement, the episomatic muscles are much reduced in volume. The musculature begins to show conspicuous longitudinal splitting while the transverse (myoseptal) splitting begins to fade. In reptiles a neck appears and there is a corresponding complexity of the anterior episomatic musculature, which foreshadows the highly complicated system of neck muscles in man.

In birds and mammals the vertebral column has the function of joining the anterior and posterior limbs and of holding up the viscera. In other words, instead of acting laterally (fish, amphibia and reptiles) the vertebral column acts dorsoventrally. Thus the lateral flexor actions become secondary to the dorsoventral flexor actions. Though the latter are most conspicuous, some of the former remain even in man. As a consequence of this change the episomatic musculature lies dorsal to the vertebral column, rather than lateral. It is reduced in volume to a great extent—one-eighth the area of the trunk instead of one-half in fish. Its locomotor function (fish, amphibia, reptiles) has nearly disappeared to be replaced by a support function, locomotion being now a function practically limited to the extremities. The head has grown larger and its movements more complicated, thus demanding more and larger neck muscles. The enormous development of the erector spinae in man, Vallois believes, is related to the assumption of the erect posture.

These are but brief excerpts from what is a very thorough and detailed account of the changes of the dorsal axial musculature in vertebrates. For those interested in the evolutionary significance in various animals of the various muscular elements derived from the simple musculature of fish, this monograph is invaluable.

KRAUS, New York.

EXPERIMENTS WITH THE USE OF THE DEFINITION METHOD IN CHRONIC PARANOID CASES. GLASER, Monatschr. f. Psychiat. u. Neurol. **51**:189 (April) 1922.

In an extensive series of experiments, with normals and subnormals, Gregor demonstrated the value of the definition method as a means of testing intelligence. The method proved more satisfactory than either of the other methods in general use—association tests or the Binet-Simon test—among other reasons, because the conditions of the experiment are well controlled and clearcut; what the person to be tested has to do can be easily explained, and the demands are relatively simple. In addition, Gregor feels that from these tests one can draw a number of conclusions regarding the psychic state of the patient.

The author has tested out Gregor's method to determine whether by its use one can get a general idea of the personality and constitution of the patient and a rapid survey of mental abnormalities. He took as material for study fifty-two patients (twenty-seven men, twenty-five women), all of whom had long been under institutional care. In most of the cases the diagnosis read "dementia paranoides"; a few, following the older nomenclature, "paranoia" or "paranoia chronica"; a few were diagnosed as "paraphrenia."

The tests were made as follows: The patient was told to explain the test words in such a way as to make them clear to someone unfamiliar with their meaning. This was usually sufficient; occasionally when one had to wait a long time and it was evident that the delay was due to consideration and not

to inhibition, the task was made easier by putting it in more concrete form, as—"What is a cloak for?" The series of test words was that used by Gregor, and in the following arrangement:

I	II	III	IV
Chair	Arm	House	Work
Cupboard	Leg	Tent	Exchange
Table	Eye	Arbor	Pledge
Cloak	Lung	Ship	Order
Tube	Mouth	Door	Lease
Boundary	Brain		

V	VI	VII
Alliance	Explanation	Burden
Calorie	Purpose	Courage
Community	Cause	Justice
Law	Contradiction	Sympathy
Authorities	Judgment	Custom
		Offence
		Transgression
		Revenge

The reaction time was not measured. The point of these studies was not to determine an intelligence defect but to see whether the method would give an insight into the psychic mechanism of the patient and discover latent delusions or complexes.

Of the twenty-seven men, 78 per cent. showed many typical schizophrenic symptoms in their reactions; 22 per cent. showed relatively few; none were entirely free. Of the twenty-five women, 64 per cent. showed much that was typical of schizophrenia in their definitions; 30 per cent. showed less; none were entirely free.

Before making the test, a general survey of the present condition of the patient was made. This survey divided the patients into two groups: those who gave a schizophrenic picture in the first words they spoke. Many of these in their definitions gave all the classical signs of schizophrenia, on the associative as well as the affective side, and the whole personality showed up in the chart. In the second group—these were all cases in which long observation had clinched the diagnosis—it was hard to make the diagnoses from the status praesens, even after long talks with the patient. Many of these cases also showed typical schizophrenic definitions.

In summary: The author feels that it is possible by the use of the Gregor method to get a rapid and accurate orientation in the group of patients studied. All the typical schizophrenic symptoms, both those on the associative side and those on the affective side, come out clearly in the definitions. The method proved of especial value in that group of cases in which the diagnosis—though established through a long period of institutional observation—was not obvious at the time of the examination. He found it of great value in showing up hidden complexes or delusions and giving an insight into the psychic state of the patient, his personality and character.

SELLING, Portland, Oregon.

THE MECHANISM OF THE ACTION OF THE SALTS OF BORON IN THE TREATMENT OF EPILEPSY. G. CUNEO, Not. e riv. di psichiat. **3**:511, 1921.

The theories on which Cuneo bases his treatment of epilepsy have been abstracted for the Archives (**9**:488 [April] 1923). The great problem has been to reinforce the alkalization function of the small intestines and the liver. At

first, Cuneo used sodium and ammonium carbonate in gelatin tubes or capsules, or in pills coated with keratin, stearin or collodion. This was to preserve the alkalies in their passage through the acid contents of the stomach. In order to check the efficacy of this treatment, the reaction of the feces was tested; the reaction, however, was maintained at an alkaline level by these means with great difficulty. Urea and the isocyanate of sodium were also used with varying results. Cuneo's second great objective was to provoke a leukocytosis so that the white blood cells might enter into a harmless union with any free proteoses present in the blood of an epileptic during the convulsive phase. The problem, therefore, has been not only to render the gastrointestinal tract alkaline and keep it so, but also to produce a leukocytosis. The fact that a leukopenia occurs just before and during the attacks in epileptics has been known for a long time and, in view of Cuneo's explanations, the reason is clear. In the therapeutic tests carried on by Cuneo and Vidoni, the basic phosphates have proved to be better alkaline substances than either the sodium or ammonium carbonates. Urea simply becomes ammonium carbonate in the small intestine by hydration and is not more efficient than ammonium carbonate. The isocyanate of sodium has been of value, but not as efficient as disodium phosphate. The borates may be ideal substances, since they are classified as alkalies and antacids, despite the fact that they have basic properties. In this respect they are like the hydrates, carbonates, phosphates and soaps, and are able to fulfil the first important antiepileptic requisite. Secondly, the borates cause irritation of the stomach and small intestines, and, depending on the dose, this irritation may become so severe as to give signs of toxicity. The irritation of the intestinal mucosa stimulates the oxidation of salts and acids into sodium carbonate which is precisely the function disturbed in the epileptic. Not only this, but the slight irritative or inflammatory process which the borates produce undoubtedly causes an increase in the number of leukocytes in the villi of the intestines. The leukocytes, rich in nucleic acid, combine with the proteoses to produce a harmless nucleohistone. The action of the borates in this regard, is identical with that of disodium phosphate, the latter having a mildly laxative action. Cuneo does not believe that the borates can be used safely in sufficiently large doses, since they produce troublesome exanthematous eruptions. This same objection holds with the borotartrate of potassium recommended by Pierre Marie which has therapeutic value only because it contains boron. It is probably less desirable because the epileptic organism is incapable of transforming alkaline tartrates into carbonates. The epileptic cannot prevent the potassium tartrate from entering the circulation, and, experimentally, potassium tartrate injected into animals causes convulsions. The author feels that the treatment of epilepsy cannot be placed on a firm foundation until all the facts of the pathogenesis of this condition are finally cleared up. He takes up briefly the apparently favorable action of scammony, jalap and senna, etc., in some cases of epilepsy, ascribing this to the fact that these substances irritate the small intestines and produce leukocytosis. He also mentions briefly a number of cases of epilepsy that improved when the patients were affected with inflammations or abscesses; probably for the same reason.

OSNATO, New York.

SYMPTOMS AND PATHOGENESIS OF PSEUDOBULAR PARALYSIS. WARTENBERG, Monatschr. f. Psychiat. u. Neurol. **51**: (May) 1922.

The author reports two interesting cases of pseudobulbar paralysis, differing in their essential characters, but having in common two unusual features: complete anarthria, and complete absence of involvement of the extremities.

Case 1.—A man, aged 27, at the age of 10 months had suffered an acute febrile affection with convulsions. With this there developed paralysis of the legs, which cleared up in two or three years, and a marked glossolabiopharyngeal paralysis that persisted. There was complete anarthria. The bulbar reflexes were exaggerated; there were no trophic disturbances and the electrical reactions were normal. There was no forced laughing or crying; the facial muscles were not emotionally overexcitable and relaxation was prompt. Mimesis was reduced.

The whole picture is that of a pseudobulbar paralysis developing on the basis of an acute encephalitis. Such a picture may result from a bilateral involvement of the corticobulbar tracts at any point in their course. In the case described, absence of psychic manifestations, of intelligence defects and of epilepsy point to a pontile rather than to a cerebral localization. The absence of pyramidal tract symptoms suggests that the lesions must have been small and have affected the fibers after they had left the pyramidal tracts proper and were crossing the pons to reach the pontile nuclei.

It is of interest that this patient was alive after twenty-six years in spite of the difficulty in swallowing, a difficulty which, in adults, is usually the cause of death. When the swallowing act is withdrawn from cerebral control early in life, as was the case here, it probably acquires a greater independence, and this may be the reason why juvenile pseudobulbar cases live much longer than adult cases. The complete and permanent anarthria is also probably related to the fact that the lesion occurred early—before the patient had learned to talk.

Case 2.—This is a case described by Wexberg, which subsequently came under the observation of the author. The patient was a girl, aged 16, who developed typhus fever during an epidemic of the disease in 1920. Defervescence occurred in the third week. Shortly after, a rise of temperature of three days' duration took place, during which the present symptoms developed: (1) complete anarthria; (2) difficulty in chewing and swallowing; (3) salivation; (4) ptosis, and (5) convulsive laughing. All the symptoms subsequently improved excepting the anarthria—this persisted unchanged. Once she talked in her sleep.

In this case, such voluntary movements as were possible in the affected region were carried out slowly and with visible effort. As the movement continued, it became easier and gradually developed normal power. There was a tendency to persistence of muscle contraction. The bulbar reflexes were not exaggerated. There was no muscle atrophy. There were no changes in the electrical reactions. Passive movements met with uniform resistance throughout. The slightest emotion would start a forced, stereotyped laugh, which began quickly, could not be voluntarily overcome, disappeared slowly, and lasted much longer than the affect. Accompanying the laughter was a spasm of the orbicularis palpebrarum, which may well have been an associated movement. The contraction would persist and relaxation was slowed.

In this second case we have a glossolabiopharyngeal paralysis with all the symptoms of a striate lesion: tonic spasm without exaggeration of reflexes, persistence of contraction, and hypermimia. The extensive involvement of the pontile muscle group, with a sparing of the extremities, suggests that a fine localization exists within the corpus striatum.

These two cases, in spite of the similarity of the general picture, present widely different pathology. The one case represents a corticospinal lesion, the other a striate lesion.

Selling, Portland, Oregon.

THE PULMONARY SEGMENT REFLEXES. JESSE G. M. BULLOWA, Am. J. Med. Sc. **166**:565 (Oct.) 1923.

Areas of hyperalgesia, which he terms pulmonary segment reflexes, have been found by the author in certain acute pulmonary conditions. In pulmonary diseases, two distinct groups of segment are involved: the cephalic group, which extends from the third cervical to the second thoracic, thus including the upper extremity, and the caudal group, which consists of and usually involves the seventh thoracic and adjacent segments. Bullowa has found an increased muscle tone over these segments due to irritative processes within the pulmonary cavity. The cutaneous reactions have been of variable intensity, but usually are present to some degree.

The author shows the origin of this reflex distribution to be directly traceable to the embryonic anlage of the lung. The cephalic representation, of course, appears in the development of the lung bud, which becomes the visceral portion of the lung. In the fourth or fifth week of embryonic life, the lung bud appears as an outgrowth on the anterior surface of the gut, at the level of the third cervical segment, which corresponds with the sixth somite. He points out that it has been shown recently that the vascular system has just as definite a phyletic plan as has the development of the nervous system, which is contrary to the old view that blood vessels followed organs as the need for them arose.

The caudal pulmonary segment is distributed to the vascular bud formed from the primitive postbranchial plexus into which the pulmonary bud advances. It is, therefore, this vascular bud, formed from these primitive arches (a relic of some primitive vertebral type in which the entire gut participated in respiratory exchange), which forms the network of vessels about the alveolar spaces, and since its somatic derivation is around the seventh dorsal segment, the caudal reflex group becomes entirely a vascular reflex.

The cephalic group of reflexes makes its appearance simultaneously with lesions of the lung, as in bronchitis, pneumonia, either lobar or lobular, tuberculosis, and laryngeal or bronchial diphtheria.

The vascular, or caudal, reflex may appear or disappear independently under certain conditions, as in asthma. Depending on whether the visceral or the vascular reflexes predominate, we obtain a cephalic or caudal type in emphysema.

Clinical conditions causing distensile pressure in the pulmonary vascular bed give rise to increase in muscle tonus corresponding to the seventh thoracic segment with some hyperalgesia over this area.

In passive congestion of the lungs, there is always present seventh thoracic hyperalgesia, which disappears when the congestion is relieved, by either reduction of blood mass, fluid intake, Karell diet or as the result of improvement of the peripheral pulmonary circulation from rest and stimulation. There is also a diminution of the muscle spasms of the segments involved.

In asthmatics, there is a typical vascular hyperalgesia, and increase of tone of muscles innervated from the caudal segments, as shown by the very great dimunition of vital capacity. Hyperalgesia and muscle spasms disappear about six minutes after hypodermic administration of epinephrin.

The author brings forth many interesting clinical observations to bear out his theory and concludes that the pulmonary bud springs from the anterior esophageal wall and grows into the postbranchial pleuxus; a separate visceral and vascular segment representation results and is of semeiologic importance.

TEMPLE FAY, Philadelphia.

EPIDEMIC ENCEPHALITIS WITH THE SEMBLANCE OF DEMENTIA PRAECOX. G. DENY and M. KLIPPEL, Rev. neurol. **29**:402 (April) 1922.

The purpose of this article is to show that a patient who has epidemic encephalitis with inflammatory symptoms does not develop dementia praecox as a sequela. In other words, epidemic encephalitis is not an etiologic factor in dementia praecox. The authors attempt to establish this thesis on the basis of clinical, anatomic and pathologic reasoning, which will be given later. Their conclusions are grounded on the study of one patient, a girl aged 16, who was admitted to the hospital of Tenon in November, 1921. The onset of the illness had been sudden, on Dec. 31, 1919, and marked by delirium, somatic hallucinations and increased psychomotor activity.

The progress of the illness briefly was: delirium with an hallucinatory episode, inactivity bordering on stupor, slight fever, passing or ephemeral diplopia and choreiform movements. At first it was thought to be a case of epidemic encephalitis. The physicians were about to do a lumbar puncture, when the patient suddenly appeared to recover. She was discharged from the hospital and sent to the country. Two months later she was returned to the hospital, when choreiform movements were in evidence, both general and localized. They lasted for nearly a year. At the same time the psychic picture became more pronounced, being characterized especially by the loss of voluntary psychomotor activity and by certain symptoms suggestive of hebephrenic-catatonic dementia praecox. In August, 1921, she was seen in consultation with Dr. Netter who made a diagnosis of epidemic encephalitis. At the time of the writing of the article she still manifested symptoms characteristic of this disease, particularly a tendency to somnolence from which she could be aroused.

After the second admission, a lumbar puncture was carried out. The cell count was four, the globulin test negative.

The reasons against regarding dementia praecox as a sequela of epidemic encephalitis then follow. First, what might be termed "analogies" in the two disorders are considered, such as the more or less complete disappearance of voluntary activity as opposed to the appearance of automatism. The authors admit the occurrence of similar or analogous symptoms, but affirm that the origin of each is different in the two disorders. In encephalitis the lowered psychomotor activity is secondary to cerebral sluggishness, accompanied by psychic asthenia and by fatigability which renders the lightest occupations difficult or impossible. In dementia praecox there is a purposeless, mechanical, automatic tendency, without ideation. The encephalitic man strives to overcome his mental sluggishness, sometimes with at least limited success; the dementia praecox patient is apparently indifferent to and rather irritated by the world of reality.

From the anatomic point of view more serious arguments can be given against regarding dementia praecox as a resultant of encephalitis. The lesions in dementia praecox are cortical and affect the highest faculties, involving especially the nerve cells and the neuroglia, as well as invading the meninges and the interstitial structures. In epidemic encephalitis the lesions are subcortical as well as mesencephalic; as in general paralysis there is an invasion of the meninges and the nerve centers (nuclei?). Sometimes the vascular and perivascular tissues are involved. In dementia praecox the lesions are usually more destructive and irreparable than those of encephalitis.

It is in the pathogeny of the two diseases, however, that we have the most distinctive differences. The infections or the accidental intoxications which

make up the syndrome of dementia praecox are apparently too light to stimulate the blood vessels to leukocytic proliferation or to produce irritation of the meninges. On the other hand, encephalitis does not interfere with the function or morphology of the cells of the cortex. Encephalitis precipitates psychotic conditions which are only incidental. In dementia praecox the psychosis and its effects on the higher cerebral functions are more or less permanent, hence the great error in regarding dementia praecox as an end result of epidemic encephalitis. The pathologic histology and the etiologic factors are essentially different, no matter how close the analogy of the clinical symptoms.

In conclusion, it should be noted, at least, that while the authors have written a stimulating paper on a much mooted question, their conclusions seem to be based on generalizations from other workers rather than on their own case. At the time of writing, their case still showed the dementia praecox-like symptoms. What it may show at necropsy is still to be determined.

JONES, Detroit.

THE QUESTION OF THE HEREDITARY OCCURRENCE OF MULTIPLE SCLEROSIS. Monatschr. f. Psychiat. u. Neurol. **51**:226 (April) 1922.

There are in the literature a number of cases of multiple sclerosis in which a hereditary or familial occurrence has been demonstrated. These cases represent such a small fraction of the total number that one is justified in asking whether the reported cases have not some other origin, bearing merely a symptomatologic resemblance to multiple sclerosis.

A number of writers, among them Marburg, Strümpell and Jendrassik, feel that the cases so far reported are inconclusive. In the recent literature, notably in the work of Kuhns, Steiner, Siemerling, Raecke, Westphal and others, evidence has been brought out suggesting that multiple sclerosis is an infectious disease of spirochetal origin. Siemerling has demonstrated living spirochetes (dark field method) in cases examined soon after death. Bullock has produced a spinal disease in rabbits by injecting spinal fluid from a typical case of multiple sclerosis; Steiner has demonstrated spirochetes in liver tissue of animals inoculated with the organism; Siemerling and Raecke believe that the plaques are inflammatory in origin; Westphal in three cases found Stäbchenzellen and plasma cells.

These observations, if confirmed, would transfer multiple sclerosis from the endogenic to the exogenic group. As yet, they have been received with much skepticism. As Nonne points out, we know of no pathogenic spirochete which is not infectious, which does not appear endemically or epidemically and is not transmitted by heredity. Strümpell points out that there is no obvious portal of entry; that the factor of infection (contagion) is lacking; that it does not occur in families and never occurs endemically or epidemically; that there is no fever and that the fluid changes are very slight. Further, we must account for prodromal symptoms sometimes reaching far back into childhood, such as a transient amblyopia without demonstrable anatomic changes, followed by long symptom-free periods. Pathologico-anatomically in favor of an infectious process are the evidences of an exudative infiltration about the blood vessels; against it, the sharp contours of the plaques, the long persistence of the axis cylinders and the slight tendency to contraction; finally, the fact that after years the disease remains confined to one organ, the central nervous system. The dispute must remain unsettled for the present. Meanwhile, the author returns to his discussion of familial occurrence of the disease. He reviews

briefly the nine groups of cases which he has found in the literature, in some of which the diagnosis was confirmed postmortem, and then records the observations in the Charité.

Case 10.—Two sisters were affected. In one, the symptoms were characteristic; in the second, less marked. In both cases the diagnosis was confirmed at necropsy. The paternal grandmother died at 35 of a spinal disease, the nature of which was unknown.

Case 11.—A brother and sister were observed in the clinic. The clinical diagnosis in both was multiple sclerosis. According to the history (obtained from the father), the mother died of a similar disease at the age of 32 after being ill seven years. The grandmother stated that five brothers and sisters of the mother died of the same disease.

Case 12.—Two sisters were under observation in the clinic; in both the cases were diagnosed as multiple sclerosis. The father developed spinal disease at 30 that was suggestive of multiple sclerosis. Two brothers and a sister of the father died of a similar disease. The grandfather also was said to have had it.

In this last group, the hereditary or familial character is especially striking. However, there are certain features of the cases which suggest the possibility that they may belong to the Friedreich's ataxia group—perhaps a combination of the spinal with the Pierre Marie type. Strümpell calls attention to the difficulties of diagnosis as between multiple sclerosis and hereditary cerebellar ataxia, and points out that the hereditary character of the latter is an important point. But the occurrence of hereditary cases of multiple sclerosis, as pointed out in the article, suggests that at times the differential diagnosis will be possible only at necropsy.

Case 13.—A case under observation in the clinic. The diagnosis was multiple sclerosis. According to the history, the father developed a similar disease at 30 and died at 43. One paternal aunt had the same disease.

Case 14.—This group includes three brothers, observed in the Charité and reported by Cramer in 1914. The ages were 14, 10 and 9 years. In this group, as in the preceding, there was some question as to differential diagnosis, as between multiple sclerosis and a heredodegeneration of the Friedreich's ataxia type.

Selling, Portland, Oregon.

A Contribution to the Study of Hepatolenticular Degeneration. A Case of Kinnier Wilson's Disease. Raviart, Vullien and Nayrac, Rev. neurol. **30**:97 (Feb.) 1923.

The case reported is that of a man, aged 18. At 12 years of age, during the German occupation of Belgium, he was severely frightened on two occasions by German officers who on one occasion struck him in the face with the hand, and on another beat him over the head and chest with a riding whip and at the same time turned loose on him a ferocious dog. His fright was so intense that he urinated involuntarily. Shortly after this he was frequently restless at night and often urinated in bed. He also on several occasions started to run away from home. By the following February (1918) he began to manifest a peculiar gait (walking on tip-toes), he spoke with difficulty and he was given to spasmodic laughter. In October, 1920, his father made application for a pension for the patient. His medical certificate at that time described him as suffering from "locomotor-ataxia with violent spasms of the muscles of the legs and with pronounced pes equinovarus."

In 1922, he was examined by the authors. He appeared unusually large for his age (17). There were striking stigmata of degeneracy, including coarse wooly hair, eye-brows meeting in the midline, and widely flaring ears. From head to foot he was practically in tonic spasm. The legs were in rigid extension, the knees were pressed firmly against each other, the feet immobile; the arms were semi-flexed, the hands open, and the fingers were in almost continuous creepy athetoid movement. The patient could not lift himself from the bed. Touching him threw him into a posture of opisthotonos—almost approaching tetany. He could not assume the sitting posture as he was unable to flex the trunk on the thighs. This complete hypertonicity was not accompanied by paralysis or atrophy. The hypertonia was somewhat spasmodic in character, and might be styled "cog-wheel movement," in which a motor act might be suddenly stopped by any attempt at passive movement, then suddenly resume itself, when movement would then go on until spasticity again suddenly intervened.

Voluntary movement was equally affected. He could not rise from his bed, move the tongue or even swallow. His food had to be liquid. Speech became progressively unintelligible. There was also marked spasm of the sphincters of the bladder and rectum. At times there were jerky rapid movements questionably voluntary such as a firm grasp on some part of the clothing of the examiner. The grip was difficult to loosen. The movements were not choreiform, but rather athetotic in character. There never was tremor nor even dysmetria when voluntary movements were still possible. The face was mask-like and the mouth half open. There was no drooling. The face was animated at times with an inexpressibly horrifying sardonic expression.

There never seemed to be any distinct psychotic manifestations. When the patient could express himself in the least degree intelligibly he seemed to show a tranquil, self-possessed mood.

Studies of the reflexes were made difficult because of the hypertonia. Those of defense could not be reported satisfactorily. The cutaneous reflexes were in the same relative state, except that there seemed to be a bilateral Babinski phenomenon. The tendon reflexes were, as far as could be determined, unchanged. There was no ankle clonus. Sensibility seemed unaffected. All the eye tests for movement and reflexes, including the appearance of the fundus, gave apparently normal results. Lumbar puncture gave negative findings in every respect. Respiratory, cardiovascular, and intestinal findings were all negative. There was incontestible evidence of atrophy of the liver. On percussion, normal dulness within the usual limits was wanting.

In recapitulation, the patient showed a syndrome consisting of a normal development in childhood; a muscular hypertonia, extreme and general in character, together with spasmodic movements and coexistent with a considerable diminution in the volume of the liver.

The rest of the paper deals with the differential diagnosis. Multiple sclerosis and infantile diplegia are first eliminated, as well as a late Friedreich's ataxia. Next in order are dismissed the juvenile parkinsonian syndrome and a postencephalitic disorder, as well as chronic chorea. The conclusion is that the authors are dealing with a progressive hepatolenticular degeneration or Wilson's disease. Yet they have to consider what Hall has described as psuedo-multiple sclerosis of Westphal-Strümpell. Wilson desires to preserve the two disorders as separate entities. If they maintain their diagnosis of Wilson's

disease, the authors must admit that it is rare in France, not over eighty cases having been reported, and, of these, only one, reported by Lhermitte, came to necropsy confirmation by pathologic tissue study.

In conclusion, the authors raise a medicolegal question: Can psychic traumatism or emotional factors be considered in the etiology? In Wilson's disease they admit that there are two types of lesions, nervous and hepatic, including a constitutional predisposition to an abiotrophic process. They do not feel justified, however, in ruling out the emotional factor (an exogenous element), especially in view of the fact that there is no history of familial taint, of alcoholism, or of syphilis. They feel assured that the case is one of Wilson's disease in which psychic trauma possibly plays some part.

JONES, Detroit.

EXPERIMENTAL CORD CRUSHES WITH ESPECIAL REFERENCE TO THE MECHANICAL FACTORS INVOLVED AND SUBSEQUENT CHANGES IN THE AREAS OF THE CORD AFFECTED. JOSEPH F. MCVEIGH, Arch. Surg. **7**:573 (Nov.) 1923.

McVeigh produced cord crushes in laminectomized dogs and studied the mechanical factors involved in spinal cord crushes, both complete and partial, and the subsequent vital changes occurring in such injuries. It was found that, in partial lesions of the cord, there is usually not sufficient pressure to convert the cord at the site of lesion completely to pulp. In complete lesions, the gross and microscopic appearance of the cord indicates that the cord substance at the site of the lesion was reduced to a hemorrhagic pulp in each instance. As the cord is a compressible substance enclosed within a fairly firm, slightly elastic canal of pia mater, the expenditure of the pressure which has been necessary to crush the cord has forced the cord pulp and blood up and down the cord from the site of injury. Thus, if the pia does not rupture, the intrapial pressure originating in the crushed portion in these cases is transferred to the segments of the cord above and below, owing to the entrance of the pulp into these segments. The portion of the cord usually chosen by the invading pulp mass is the central gray matter dorsal to the central canal, rarely involving the central canal and the ventral portion of the dorsal white columns.

The cause for this is the weaker anatomic structure of this area as compared with other areas. When the pressure on the cord was sufficient to produce a complete lesion, the cord area involved in the pulp invasion tended to be larger above the level of the injury in the lower cervical and upper dorsal regions, and consequently more damage resulted in these regions. This is probably true also in the region of the lumbar enlargement.

Edema and hemorrhage are factors to be dealt with in partial lesion and concussions. Massive hemorrhages do not occur as a rule, and small scattered hemorrhages are most often observed. These are probably not extensive enough to produce serious injury of themselves. Edema comes on within eight hours and attacks the dorsal white columns principally, but it is frequently quite marked in the lateral and anterior columns as well. Time is a factor, since edema seems more marked in proportion to the length of time the dog lives. A marked intrapial pressure is developed as the result of the edema. This becomes more evident when the dura and pia are incised and this pressure is released. Judging from the case in which the dura was nicked, it seems that operative procedure would cause a further destruction of the cord substance without relief of the edema in areas of the cord often affected. The release of the pressure seems to have no effect in checking edema formation.

The intrapial pressure forced cord substance and pulp out through the incision in the pia with such force that damage must necessarily have been done to otherwise uninjured neighboring tracts.

Liquefaction of the pulp and the area of the cord involved in the débris in complete lesions sets in after forty-eight hours; is progressing rapidly at the end of four days, and is completed within two weeks. Thus the syringomyelic cavity and symptoms above the level of the lesion and cavity below in many old cases of fracture of the spine are accounted for. The process is brought about by the rupture of or pressure on blood vessels supplying the involved area, and the pressure on the included nervous tissues which are pushed aside. The presence of an increasing number of ameboid and granule glial cells in this area suggests their phagocytic function.

GRANT, Philadelphia.

HEMITREMOR OF THE TYPE OF MULTIPLE SCLEROSIS DUE TO A RUBROTHALAMO-SUBTHALAMIC LESION. M. CHIRAY, C. FOIX AND I. NICOLESCO, Ann. d. méd. **9**:173 (Sept.) 1923.

In multiple sclerosis, and especially in its cerebellar forms, there is a sort of dissociation between intention tremor and the other cerebellar symptoms both equilibratory and coordinative. This dissociation is often of the greatest importance in the diagnosis of multiple sclerosis, but its anatomic basis has lacked exact explanation. The present authors bring illumination to the subject, however, by anatomicopathologic studies of serial sections in a case (not multiple sclerosis) having sharply focal symptoms. In this case a lesion, probably vascular, developed under febrile conditions when the patient was 8 years of age and was verified at 43. The outstanding clinical symptom had been hemitremor of the extreme intention type with only slight evidence of a rounded out cerebellar syndrome — slight dysmetria and moderate adiadokokinesis. There were nystagmus, and writing difficulties, extreme in degree and such as are common in multiple sclerosis and unsteady speech. Pyramidal signs or sensory changes were absent. There had been slight strabismus (without ocular paralysis) and also bilateral exophthalmos.

The paper, which is illustrated, details the degenerative changes that the serial sections disclosed. The degeneration of most importance was of the superior cerebellar peduncle. This extended to the dentate nucleus, but the cells of the latter were conserved. There was degeneration of both the posterior longitudinal bundle and the central portion of the tegmentum. It was not possible to find clear cut changes in the rubrospinal tract.

The syndrome of the red nucleus (the syndrome named and described by Claude) consists of cerebellar symptoms of one side with motor oculi paralysis of the opposite side. It is a sort of Weber's syndrome, but one in which pyramidal hemiplegia is replaced by "cerebellar hemiplegia." The lesion causing this syndrome is due to the obliteration of one of the median subprotuberantial arteries of Duret (among the terminal arterioles of the posterior cerebral artery), which nourishes at the same time the inferior portion of the red nucleus and the nucleus of the third nerve. The writers draw the distinction that this syndrome is actually an inferior syndrome of the red nucleus and that, in contrast, a superior syndrome of the red nucleus can be differentiated. The superior syndrome (otherwise called the rubrothalamic syndrome) follows the obliteration of a different artery, namely one of the optic arteries of Duret (other terminal arterioles of the posterior cerebral). This arteriole supplies the superior and external portions of the red nucleus and reaches the thalamus

and pulvinar. In the superior syndrome of the red nucleus there is a mingling of cerebellar signs with more or less definite thalamic features, without the oculomotor paralysis which is present in the inferior syndrome.

The writers conclude that a dissociation between intention tremor and the rest of the cerebellar syndrome (particularly the disturbances of equilibrium) is brought about by a lesion of the system of the superior cerebellar peduncle and more especially of the red nucleus and the rubrothalamic relay.

DAVIS, New York.

IS SYDENHAM'S CHOREA TO BE CONSIDERED A PROVINCE OF EPIDEMIC ENCEPHALITIS? L. BABBONEIX, Paris méd. **13**:255 (Oct. 6) 1923.

Babboneix states that the question of chorea seemed to be settled until a "star of the first magnitude appeared in the nosologic firmament," namely encephalitis. The analogy is as follows: (1) The muscular jerks of chorea are quite similar to the involuntary movements of encephalitis; (2) flaccid paralyses sometimes make their appearance in both diseases; (3) mental disorders exist in certain cases of chorea; (4) alterations in the blood and spinal fluid are similar; (5) certain choreas begin with a period of somnolence; (6) the serious forms of the two diseases run a similar course; (7) relapses are frequent in both; (8) chorea gravidarum resembles cases of encephalitis gravidarum; (9) lesions occur in the same location (according to Pierre Marie and Trétiakoff) and are of the same nature histologically; (10) according to the researches of Harvier and Levaditi the virus of cases of chorea can cause meningo-encephalitis in rabbits with the exhibition of involuntary movements of the extremities.

The author divides the arguments above noted into "cheap" and more impressive. The clinical course means little, the anatomic findings nothing more; nevertheless, biologic experiments, as the investigators admit, do not prove the identity of the two diseases. Arguments against the identity have been given as follows: (1) Chorea is a disease of early life, whereas encephalitis affects adults. This has been disproved by the numerous cases of encephalitis seen in children. (2) Chorea sets in without fever, whereas encephalitis begins bruskly with fever. Here also there are well defined exceptions to the rule. (3) The movements as a rule are different in the two diseases: "Delicate differences of appreciation; shades often impossible to catch." (4) The occurrence of arthritis and of endopericarditis in chorea. Of all arguments, this seems the most important.

Babboneix firmly believes the two diseases are different, but he admits that in the large group of childhood choreas the cases which have nothing to do with encephalitis must be carefully distinguished from those which are in relation with encephalitis. In the former we must look for arthralgias. They are not complicated by somnolence, ocular paralyses, nor by rhythmic movements; they never give rise to the parkinsonian syndrome. In six weeks the involuntary movements cease and the disease may be considered cured, unless, as too often happens, it leaves as a residual a mitral lesion or pericardial adhesions. "These are the rheumatic choreas of classical authors."

Choreas complicating epidemic encephalitis are not complicated by arthropathies, nor cardiopathies, but are accompanied by rhythmic movements, parkinsonian syndromes, and character disorders. The two disorders approach each other most closely in those states of incessant involuntary movements in which repose is impossible, delirium is constant and the progress is toward a fatal termination.

FREEMAN, Paris, France.

THE CHANGES IN AMOUNT AND DISTRIBUTION OF THE IRON-CONTAINING PROTEINS OF NERVE CELLS FOLLOWING INJURY TO THEIR AXONS. F. M. NICHOLSON, J. Comp. Neurol. **36**:37, 1923.

This investigator has demonstrated that particular nerve cells stained first by the Nissl method and subsequently tested microchemically for organic iron, present identical histologic pictures, except for the absence of such iron-containg substance in the smaller Nissl bodies around the periphery of the cell and its presence in the chromatin material of the nucleus. It is probable that the Nissl bodies contain a nucleoprotein with an iron moiety. The changes of this iron-holding nucleoprotein have been studied after ligation of the hypoglossal nerve and after tearing of the nerve external to its foramen. During the first fifteen days after ligation of the nerve there is a gradual reduction in the amount of the iron-containing material in the cytoplasm of the cells within the hypoglossal nucleus. This reduction is particularly marked immediately around the nucleus of the cell, especially on the side nearest the axon hillock. The residual iron-containing material accumulates around the axon hillock which diminishes in size. From the sixteenth to the forty-fourth day reparative changes appear. Small granules of the iron-containing substance accumulate around the nuclear membrane whence they spread toward the periphery of the cell. No changes in the distribution of the iron-containing substance have been observed in the dendrites or in the axon hillock. During the first three days the iron material in the nucleus diminishes. From the third to the eighth day it increases to an amount above normal and then again falls below normal up to the fifteenth day, after which there is a gradual return to normal. It is always more abundant on the side of the nucleus nearest the axon. No changes have been observed in the nucleolus. When the nerve is torn the retrogressive changes are slower and more accentuated, and there is no regeneration. The phenomenon of chromatolysis is a true chemical change in which there is a dissolution of the iron-containing Nissl substance, which change possibly represents an attempt by the cell, whether it be successful or not, at reparation.

GRAY, Chicago.

PHYSIOPATHOLOGY OF THE SYMPATHETIC. M. LAIGNEL-LAVASTINE, Encéphale **18**:494 (Sept.-Oct.) 1923.

In this paper the author suggests that a proper understanding of the sympathetic nervous system—by this term he refers to both the sympathetic and parasympathetic portions of the vegetative nervous system—is based on a physiologic rather than an anatomic conception. It is known that the chemical structure of the sympathetic nervous system becomes more complex as animals rise in the phylogenetic scale, and that drugs failing to act on lower forms of life produce effects on higher forms. It is in a selective chemical irritability of the various portions of the sympathetic that one can account best for the diverse and frequently antagonistic actions of the mechanisms controlling nutritive functions. Spadolini suggests that the tissue reaction of the sympathetic depends on three factors: (1) the amount of stimulating substance present; (2) the momentary state of balance of the sympathetic; (3) the chemical affinity of the stimulating substance. The disturbed function of the sympathetic may be due to gross local lesions, body tissue fluid abnormality or a pathologic state of chemical reactivity of the sympathetic.

The individuals termed "neuropathic" are characterized by an abnormal irritability of the vegetative nervous system. Each organ has normally its own proper rhythm or cycle of activity and the response of an organ to a stimulus depends, to some extent, on the stage of the cycle in which a stimulus is received. This fact, and the conception of Spadolini, account for the seemingly contradictory experimental and clinical results of drug administration.

The author criticizes the scheme of Eppinger and Hess as being too rigid and formal. He quotes from Danielopolu and Carniol the opinion that many cases commonly termed vagotonia and sympathicotonia are really hypertonia—or better hyperexcitability—of the vegetative nervous system.

Laignel-Lavastine closes with the observation that our knowledge of the vegetative nervous system is still insufficient to draw accurate clinical applications and that further clinical observation and animal experimentation must be correlated.

HYSLOP, New York.

SPINAL RADIOGRAPHY BY MEANS OF LIPIODOL. J. A. SICARD, P. PARAF and L. LAPLANE, Presse méd. **85**: (Oct. 24) 1923.

Lipiodol is a 54 per cent. solution of metallic iodin in a vegetable oil. It can be safely injected into the soft tissues of the body, remaining in situ for over two years without absorption. It is opaque to roentgen rays. Sicard has used it in several cases to demonstrate the patency of the spinal canal in cases of suspected medullary lesion. Following the suggestion of Ayer he uses the atlanto-occipital space for the injection and has experienced no unfavorable results. The patient is placed in the semireclining lateral position, with the vertebral column in a straight line and the head bent forward. As a rule he uses no local anesthetic, but introduces the needle in the midline against the ligamentum nuchae, directing it toward the occipital bone slightly. A small syringe with saline solution is provided, and in case of difficulty a little fluid is expressed, opening up the tissues. At a distance of from 3 to 5 cm., penetration of the dura is readily recognized. He estimates that about 1.5 cm. separates the dura and the medulla at this point. About 1 c.c. of lipiodol is then injected slowly, the needle is withdrawn and the patient is placed upright, after which the back is percussed to facilitate the descent of the fluid. In normal cases the solution should have reached the lumbar sac at the end of two or three minutes. The roentgenogram should be taken in the upright posture. In case of doubt a second exposure may be made a day or two later.

The authors give directions as to the injection of lipiodol at other levels of the spinal column, but believe these procedures more difficult and sometimes more dangerous than the first procedure. In a series of 150 cases of intraspinal injection, of which fifty were given in the basilar region, no casualties are reported. In nine cases an exact localization of the tumor was possible, and proved at operation to be correct. The authors cite instances of success by others in the method, and publish striking roentgenograms borrowed from Percy Sargent, Froment, Japiot and Dechaume.

FREEMAN, Philadelphia.

THE SUBNORMAL AND PSYCHOPATHIC CHILD AS EXEMPLIFIED IN A SPECIAL CLINIC. LOUIS A. LURIE, J. A. M. A. **81**:1262 (Oct. 13) 1923.

The nature of a child's conduct reactions depends on two factors: (a) his innate physical and mental capacity for reacting and (b) the nature of his

environment. Hence, when we are confronted with any form of psychopathy in childhood, both of these factors must be properly evaluated. In addition, the reactions of the child when placed in a normal environment must also be known. Provision for such observation has been made at the Psychopathic Institute of the Jewish Hospital of Cincinnati; here the effects on the child of clean clothing and surroundings, proper recreation and entertainment are noted.

Up to this time more than 150 cases have been studied and as a result of this work the author believes that enough children have been reclaimed for society to warrant the statement that it is unfair to commit any child who shows any form of antisocial behavior or conduct disorder to a corrective or custodial institution before he has been given the benefit of such a complete study.

NIXON, San Francisco.

EXPERIMENTS ON THE REVERSAL OF THE SPINAL CORD IN AMBLYSTOMA EMBRYOS AT THE LEVEL OF THE ANTERIOR LIMB. S. R. DETWILER, J. Exper. Zool. **38**:293 (Oct. 5) 1923.

Reversing the anterior limb level (third, fourth and fifth segments) of the spinal cord in *Amblystoma* embryos has no effect on the character of the developing responses to tactile stimulation. A greater percentage of normal results was obtained when the operation was performed just after the complete fusion of the neural folds than when performed just prior to the period when initial reflexes begin. The developing limb reflexes and their coördinate movements are not affected by reversing the limb level of the cord. In all cases that survived, the limb reactions were normal. Microscopic examination of sections of these larvae shows that the character of the brachial plexus and the intrinsic distribution of its branches are identical with the normal. The interchanged third and fifth segmental nerves carry on, respectively, the functions of the normal fifth and third. The character of the peripheral connections under these conditions indicates that the apparent "preference" which the normal brachial nerves show for the limb when the latter is transplanted into a heterotopic position is in no way an expression of any inherent specificity existing between muscle and nerve. Regardless of the segmental innervation to the limb, the intrinsic distribution of nerves within the appendage is always the same and is evidently dependent on the primary mode of arrangement of the other structures composing the limb. The results of these experiments strengthen the view that initial connection of the outgrowing nerves with their normal terminal systems cannot be explained on mechanical grounds alone. It appears possible that proper peripheral selectivity may be determined by some such electrochemical mechanism as that suggested by Kappers to account for selectivity within the central nervous system.

The extent of cellular proliferation within the various segments of the limb level of the cord in normal development is not maintained in the experimental animals with reversed cords. The reversed fifth segment undergoes cellular hyperplasia approximately equal in extent to that which characterizes the normal third segment, whereas in the reversed third segment, incomplete development follows and the degree of cellular differentiation approximates that which typifies the normal fifth segment. These results suggest that the normal gradient of cellular differentiation within the anterior limb level of the cord is commensurate with the number of longitudinal correlation fibers normally ending in these various levels for the coordinate control of the limbs. More evidence

has accumulated in these experiments to indicate that the various segments of the cord are capable of remarkable readjustment and adaptation to experimental conditions.

WYMAN, Boston.

CEREBRAL LESIONS AND DIABETES MELLITUS. CAMUS, GOURNAY and LEGRAND, Paris méd. **13**:267 (Oct. 6) 1923.

Claude Bernard discovered that injury to the floor of the fourth ventricle produces temporary glycosuria in animals In the region of the tuber cinereum, the authors obtained some positive results, in rabbits, of much longer duration. The most successful experiment resulted in glycosuria from August 22 to October 7, the urine at one time containing nearly 7 per cent. of sugar. Glycosuria always appeared late. In the case cited it appeared after six weeks, and was quite temporary. There were numerous negative results. Necropsies showed lesions of the hypophysis in many cases, but the authors refer to the work of Camus and Roussy who obtained glycosuria in dogs without injury to the hypophysis. Some of the animals showed extreme polyuria, voiding half of their body weight in twenty-four hours.

FREEMAN, Paris, France.

SPONTANEOUS CURE OF A CASE OF EPIDEMIC (LETHARGIC) ENCEPHALITIS FOLLOWING AN ATTACK OF PNEUMONIA. J. H. LEINER, J. A. M. A. **81**:1284 (Oct. 13) 1923.

A boy, aged 8 years, had an attack of encephalitis in September, 1919; a month later he manifested symptoms of reversal of sleep, change in character, and other disturbances and a year after the onset of the disease he developed paroxysmal attacks involving the respiratory mechanism and a complete change in behavior. Following a frank lobar pneumonia a few months later the respiratory attacks ceased entirely and for nearly the past year and a half he has been free from attacks and his conduct is excellent, a striking contrast to conditions during his illness.

Since this observation the author has used as a therapeutic measure, a nonspecific protein in the form of sodium nucleinate in more than twenty-four cases with gratifying results.

NIXON, San Francisco.

A COMPARISON OF THE CEREBELLAR TRACTS IN THREE TELEOSTS. W. H. F. ADDISON, J. Comp. Nuerol. **36**:1, 1923.

This article is timely in view of the revival of scientific interest in the cerebellum. The cerebellar connections of the codfish, a flat-fish, and a species of siluroid fish are reviewed and differences noted which are correlated with the habits of the respective animals. In all of these cerebellums there is a prolongation forward into the anterior medullary velum, the valvula cerebelli, which receives fibers from the vestibular and lateral line nerves and centers. This probably represents a derivative of the oldest part of the cerebellum. To this is added the body of the cerebellum which receives fibers from the spinal cord bearing both proprioceptive and exteroceptive impulses, from the hypothalamic region probably bearing gustatory and olfactory impulses, from the vestibular centers in the medulla, and from the optic tectum, a visual reflex center. These tracts were studied comparatively with results of which the following are typical examples: In the cod which has very large eyes and

optic lobes there is a large tract from the optic lobes to the cerebellum; in flat-fishes and siluroids with smaller eyes this connection is smaller. The spinocerebellar tracts are larger in the two species last named, whose body and fin musculatures are larger than in the cod.

Two pathways descend from the cortex of the cerebellum to the brain stem: one derived in part from the valvula running cephalad and the other from the body of the cerebellum running caudad. The former is probably homologous with the brachium conjunctivum. The cerebellum in these animals functions, then, not only through its connection with the proprioceptive system, but also through those with the exteroceptive and interoceptive systems.

GRAY, Chicago.

DECOMPRESSIVE TREPHINATION AND VENTRICULAR PUNCTURE. J. A. BARRÉ and P. MORIN, Paris méd. **13**:252 (Oct. 6) 1923.

The authors undertook the measurement of spinal fluid pressure during and after decompressive operations. They found that the fall began as soon as the first trephine opening had been made, but that recovery was rapid and the pressure remained high for a number of days, almost as high as before operation. The relief of symptoms was remarkable in the advanced cases in which it was undertaken. The stand taken by the authors is that the headaches are due to crises of higher tension and that the deliverance of the dura from its rigid case permitted a sort of safety-valve action. Ventricular puncture, and ventricular drainage when it can be accomplished, present the surest means for relief of the intracranial hypertension and are relatively safe procedures.

FREEMAN, Paris, France.

MYASTHENIA GRAVIS: REPORT OF A CASE. A. S. JACKSON and A. D. BATES, J. A. M. A. **81**:114 (July 14) 1923.

The case reported is that of a man, aged 26 years. There was general muscular asthenia but the greatest involvement was in the ocular and laryngeal groups of muscles, and in those governing deglutition. He was placed at absolute rest, and strychnin was given in increasing doses until he was receiving as much as one-fourth grain (0.015 gm.) hypodermically four times a day. Early improvement was noted in the muscles of phonation, mastication and deglutition.

NIXON, San Francisco.

Society Transactions

NEW YORK NEUROLOGICAL SOCIETY

The Four Hundred and Eighth Regular Meeting, Dec. 4, 1923

E. G. Zabriskie, M.D., *Presiding*

MYOTONIA. Dr. M. Neustaedter.

Dr. Neustaedter presented a boy, aged 11, who had myotonia. He was previously presented five years before. The parents were cousins. There was no response to either the galvanic or faradic current in the lower extremities. There was a marked hypotonia, but no muscle wasting. The Wassermann reaction in the blood and spinal fluid was negative. The involvement was simply that of one of the lower extremities. The boy improved remarkably until he had an attack of double pneumonia. The loss of response to galvanism and to faradism is hard to account for. He had no sensory disturbances. I had also two other cases under observation. The patients died. In these, all muscles were involved; but there was no wasting.

TWO CASES OF JUVENILE PARESIS. Dr. Charles Rosenheck.

Case 1.—A young woman, aged 17, the elder of two children, the other died at the age of 5 from an acute surgical condition, two weeks after birth developed a rash which yielded to mercurial rubbings. She walked at the age of 2, teethed and talked early. She had no serious illness; began school at the age of 7, but was "left back" a number of times. At the age of 16 the teacher, struck by her apathy and lack of understanding, referred her to a clinic where a diagnosis of neurosyphilis was made.

According to the mother, the patient had for a considerable time shown marked hebetude, but no gross disturbance in conduct, judgment, orientation or memory. Her mother thought her memory was good. She was docile, accepted orders without protest and was well-behaved. A year ago she developed lancinating pains in the lower extremities and occasional headaches. Quite recently, an apoplectiform seizure produced an aphasia and confusional state, which disappeared in a few days.

Examination revealed pupillary rigidity, negative fundi, tremor of the hands, tongue, lips and facial muscles, a slight Romberg sign, hyperactive deep and superficial reflexes. The blood Wassermann test was strongly positive, and the spinal serology was typically paretic.

Case 2.—A boy, aged 9, was the second child, the first having died of an intercurrent affection. There were three other children, aged 8, 7 and 4 years, apparently in good health and with negative blood Wassermann tests. There was no history of miscarriages. Birth and early development were apparently normal. At 5 months, however, the patient developed a rash on his legs, which disappeared after medication. Walking and talking developed at the proper time. At the age of 6, he started school and seemed to get along well for about one year, then his teacher noted his inability to grasp rudimentary class work. His memory showed grave defects, as he would forget to go home and frequently

was found wandering away in an aimless sort of manner. This state had continued for the past two years. About one and one-half years ago speech defect became evident, and increasing failure of memory and deterioration manifested themselves. He wet and soiled himself quite often, expressed no wishes or desires, and showed apparently no spontaneity in thought or action.

Examination revealed a gait which was slightly ataxic, a slurring paretic speech, pupillary rigidity, labiolingual tremors and hyperactive deep and superficial reflexes. The blood Wassermann test was positive, and the spinal serology was typically paretic. The father showed a positive Wassermann test. The mother refused to have a blood test performed.

Comment.—Juvenile general paresis occurs more frequently than we have been aware of.

A number of cases are apparently the formes frustes type. As these cases are usually placed in the indeterminate neurosyphilitic group, this may in a measure account for their lack of recognition.

Juvenile general paralysis is the product of a prolific and degenerate stock, plus a congenitally acquired syphilis.

The clinical picture of general paralysis in childhood or youth is rarely as typical as that of the adult. This is obviously due to incomplete cerebral development and insufficient mental acquisitions. In the main, however, the symptomatology differs little from the adult forms. Two marked features are, however, present in the juvenile forms which are worthy of mention. These are entire absence of grandiose ideas and early and progressive deterioration.

DISCUSSION

DR. J. SMITH: I think that a thorough mental examination is necessary before making a diagnosis. Progressive deterioration or a poor memory is not enough. Is the memory really affected so that the patients do not remember dates, or is there a general lack of attention? I do not favor a diagnosis of paresis in the cases presented.

DR. J. H. GLOBUS: I would like to ask why the doctor made a diagnosis of general paresis. What is there in these cases more than congenital syphilis with involvement of the central nervous system? What justifies a diagnosis of juvenile paresis?

DR. L. H. CORNWALL: There does not seem to be a great amount of deterioration in the girl, considering the length of time she has had this condition. How long has Dr. Rosenheck had these patients under observation? What was the treatment and what was the effect of treatment? The young boy does not show great deterioration, and I think we might doubt the fact of general paresis. One might even expect considerable improvement in the girl's case. I should like to ask about the serology of the parents. Paresis in children does not show the same mental changes as in adults because they have not the same psychic background. I think these are straight cases of congenital syphilis, and the young boy has probably parenchymatous syphilis in the cells of the cerebral cortex. Whether these cases are paretic is open to doubt.

DR. E. D. FRIEDMAN: I have seen taboparesis in a boy of 14, corresponding to the type of that of the younger patient. It started with a tabetic picture with loss of reflexes, then rapid mental deterioration, convulsive seizures and optic atrophy. The spinal fluid was positive. That case had the features that Dr. Rosenheck has shown here: involvement of the base of the brain and hypothalamic region which is an important vegetative center. The condition of the

young girl is not typical dementia paralytica. The convulsive seizure suggests paresis. The boy is said to show no grandiose notions, but the psychic content of the child's mind is not capable of building up an elaborate structure, as is that of an adult. The length of the disease is easily explained as it takes ten or twelve years for congenital syphilis to appear in the nervous system. In this boy there do not seem to be evidences of Hutchinson's teeth, or of keratitis.

Dr. P. R. Lehrman: Euphoria in paresis is rare. Psychiatrists have difficulty in pointing it out in this syndrome. I doubt very much that the girl has paresis. A thorough mental test should be made.

Dr. I. J. Sands: In regard to grandiose notions, these children use very bad "cuss words," which in a way is the childish substitute, and this language shows in what manner they are affected. The instinctive side of their nature is precocious. Intelligence tests on these patients are misleading, because they are far ahead in certain things. Judgment is as a rule weak. Treatment does not do any good in these cases.

Dr. Rosenheck: Adult cases do not always show clear-cut pictures, which should be emphasized. Juvenile paresis is long drawn out, with slow deterioration. I would emphasize what Dr. Sands said about intelligence tests. The serology is negative in the girl's parents, but she had a syphilitic rash at birth. The boy's father had a + + + Wassermann reaction. I have no doubt that on the East side, where Dr. Sands works, the children use pretty bad language.

INVOLUNTARY MOVEMENTS: THEIR UNUSUAL ASSOCIATION AND RELATION OF DYSKINETIC AND EXTRAPYRAMIDAL SYNDROMES TO THE PHENOMENA OF DECEREBRATE RIGIDITY.

Drs. S. Brock and I. S. Wechsler.

The following cases were shown from the Neurological Service of Montefiore Hospital:

Case 1.—A girl, aged 18, developed a choreiform, parkinsonian, and tick-like movement after epidemic encephalitis. There was also an hysterical astasia-abasia and one year after the acute encephalitis she showed bilateral ptosis, nystagmus and slight weakness of the right side of the face in addition to the hyperkinetic phenomena above mentioned.

Case 2.—A woman, aged 28, married, suddenly developed an involuntary movement confined to the musculature of the right foot, which consisted of a slow, dystonia-like fanning of the toes by plantar flexion. This interfered with walking. Occasionally the toes exhibited a tremulous movement. There was no history of antecedent disease. No other symptoms or signs were present, and the condition had remained stationary for the past three years. The case was not of the functional type.

Case 3.—A boy, aged 11, Italian, had a remarkable dyskinetic syndrome, following epidemic encephalitis, belonging to the dystonia group, sequential in nature and limited to the head and neck musculature. There were recurring waves of movement in which the head was greatly retracted, the back became opisthotonic, the right hand became hyperpronated, and the right foot assumed an equinus position. The whole picture formed an exquisite example of decerebrate rigidity. During the seizures (which varied considerably in frequency and intensity) there was loss of associated swing in the upper extremities. The pupils were unequal, irregular and reacted poorly to light and in accommodation. A fine, rapid, lateral nystagmus and a marked vertical nystagmus were present.

Conveyance was poorly done. The tongue deviated to the left and showed coarse tremors and fine fibrillations. There was hypertrophy of the sternomastoid and shoulder girdle musculature. During an attack these muscles were hypertonic. A respiratory grunt occurred during the seizure. There was a bilateral Babinski sign, with equal, lively knee and ankle reflexes. There was no ankle clonus; the abdominal and cremasteric reflexes were equal and active. There were no cerebellar or sensory signs. The variety of signs was indicative of the diffuse multiplicity of lesions from the basal ganglia to the medulla.

These cases indicate the peculiar associations and fragmentations of involuntary movements and reflect the serious inadequacy of the present nomenclature.

Objection is taken to Walshe's stand (expressed in his article in the July, 1923, number of the *Archives of Neurology and Psychiatry*) in which he limits the phenomena of decerebrate rigidity to *lesions of the pyramidal pathways*, excluding the extrapyramidal syndromes. The greatest objection to this concept is that a hemiplegic lower extremity, due to a lesion of the pyramidal tract in the cervical or upper lumbar spinal cord, is the same in nature, as regards posture and reflexes, as the plegic lower extremity produced by a midbrain interruption of the pyramidal tract. Of what avail is that mechanism in the pontomesencephalic region, the release of which gives us experimental extensor rigidity? Warner and Olmstead (*Brain* **46:** Pt. 2, July, 1923) have shown the significance of the pontofronto cerebellar pathway, as the inhibitor of decerebrate posture in cats. This tract rather than the pyramidal tract deserves attention in this connection. Replying to Walshe's criticism that no one has observed the presence of involuntary movements in the decerebrate animal, we would point out the unfairness of comparison between an *animal* in which a carefully planned surgical experiment has produce a sole effect, i. e., decerebrate rigidity, and *man*, in whom inflammatory and heredodegenerative diseases of long development and standing have manifested decerebrate rigidity phenomena which are only partially developed, are secondary, and do not occupy the foreground of the clinical picture. Lastly, Meyers (*Arch. Neurol. & Psychiat.* **8**:383 [Oct.] 1922) has made a careful clinical and pathologic report of two cases which showed Magnus-DeKleijn and decerebrate rigidity phenomena. In one, clinical and pathologic investigation disclosed *no lesion of the pyramidal pathway.*

We feel that one observes phenomena showing the pattern of decerebrate rigidity in dyskinetic and extrapyramidal syndromes, and that no one has conclusively shown that the *quality* of this extensor postural tonus must be the *specific* hypertonus of pyramidal tract lesions.

DISCUSSION

DR. HENRY A. RILEY: I protest against including the woman with the foot movement in this class of cases. Her disturbance seems to me to be of functional type. Either all the toes come up or go down, and I cannot conceive where such a movement can originate, except in the cortex. No disturbance in other sites could cause motor phenomena of that type. The other case is extremely interesting.

DR. WECHSLER: This paper is in answer to Walshe's criticism on decerebrate rigidity. This term is used too loosely, but it may be applied clinically to the cases presented. Dr. Riley's criticism is only partly justifiable; hysteria lasting three years would be unusual. We believe there is invasion of the basal ganglion. I believe it is dystonia, but perhaps mental examination and analysis might reveal other factors. If so, the patient would be excluded from this group.

BOSTON SOCIETY OF PSYCHIATRY AND NEUROLOGY

Regular Meeting, Dec. 6, 1923

F. K. HALLOCK, M.D., *President, in the Chair*

HEAD NYSTAGMUS IN MAN: REPORT OF A CASE. DR. C. L. WOOLSEY.

Head nystagmus in man has frequently been observed in persons with a fistula into the labyrinth. Comparatively few cases have been reported not due to labyrinthine fistula. Mygrind recently expressed the opinion that head nystagmus in man is a normal vestibular reflex, but it is of the greatest rarity. I do not agree with that statement. I believe that head nystagmus in man occurs frequently in lesions encroaching on the vestibular system. A number of cases of head nystagmus not due to fistula into the labyrinth have been observed in the nerve clinic of the Massachusetts General Hospital. Recently I saw a case that was unquestionably one of head nystagmus due to a pontile lesion encroaching on the posterior longitudinal bundle and the vestibular nuclei.

G. S., aged 12, was of average intelligence, quite diligent and good-natured. In May, 1923, he became listless, lazy, had decided memory defect; he was lethargic and slept morning and night. Vision began to fail, and diplopia was distressing. He experienced vertigo (both objective and subjective), accompanied by nausea and vomiting. Later, during the course of the disease, insomnia superseded the lethargic state. He walked toward the right anterior quadrant. Nystagmus of the eye, at times horizontal but usually vertical, was noted by the mother. She also noted that soon after the onset, a head movement "just like the eye movement" appeared. He had definite head nystagmus, usually vertical in type, with the slow component downward and forward and the quick phase upward and backward, but it was rotary, diagonal and at times horizontal. It is noteworthy that the head nystagmus was synchronous with the eye nystagmus and always like it.

The caloric tests indicated a pontile lesion. In July, 1923, his spinal fluid Wassermann test was negative, but the colloidal test showed a paretic curve. A short time later, at another hospital the colloidal gold curve was of the paretic type but not so definitely as before. Analysis of the spinal fluid on two subsequent occasions was entirely negative, the three tests at first indicating an abnormal fluid, which later became normal.

The whole picture was one of lethargic encephalitis complicated by a lesion involving the pontile and vestibulospinal tracts of the vestibular system, with a resultant head and eye nystagmus that were alike and synchronous.

A complete report of the case will appear at a subsequent time.

DISCUSSION

DR. E. W. TAYLOR: This is obviously an extremely difficult communication to discuss because most of us are not sufficiently familiar with the complicated problems which the labyrinth presents. I feel that Dr. Woolsey has added something definite to our knowledge, particularly of head nystagmus or head movements, which he is right in saying we have been inclined to put in the category of tics, or habit spasms, or possibly explaining them on some psychogenic basis. This opinion he has done much to disprove.

DR. H. CUSHING: I am glad to add my word of congratulation to Dr. Woolsey. About all we could say regarding this boy whom we saw at the hospital was: "These are cerebellar symptoms," but there is no evidence of tumor.

DR. WOOLSEY: The discomfort caused by the commonly employed tests should be borne in mind.

The tests are severe, and my object was and is to classify these syndromes so that they will be easily understood. We have some syndromes relating to quadrants of the body, and patients complain that they have a tendency to fall or are drawn into one or more of these quadrants. I am attempting to prove that these movements are due to vestibular lesions; that we do have head nystagmus in man; that it is relatively common. We have had from thirty to forty cases of head nystagmus synchronous with eye nystagmus. Torticollis is frequently due to some lesion in the vestibular apparatus (a lesion at some definite point), and needless operations on the neck and needless treatment would be avoided if we did not say that certain movements of the head were tics and of psychogenic origin. Perhaps they are not, and in the years to come somebody may classify these syndromes so that it will not be necessary to perform the Bárány tests on every patient. It is with this in view that I am conducting my experiments.

RADIOGRAPHY FOLLOWING THE INJECTION OF IODIPIN INTO THE SPINAL SUBARACHNOID SPACE. DR. JAMES B. AYER and DR. WILLIAM J. MIXTER.

One of us (J. B. A.) has previously presented before this Society a method for the determination of spinal subarachnoid block by means of dynamic studies in connection with lumbar puncture, and more especially combined lumbar and cistern puncture. While of great aid in separating spinal cord lesions due to compression from degenerative diseases of the cord, this method does not give evidence of the location of the block. The object of the employment of iodipin is not only to demonstrate a block, but also to localize it.

Some time ago we learned of the method used by Sicard with success, on which two articles have been published, one by Sicard and Forestier (*Presse méd.* **31**:493, 1923), the other by Percy Sargent in an August number of the *British Medical Journal*. The former paper deals with the use of iodipin in a number of different locations, but emphasizes its use in: (1) the subarachnoid space, and (2) the epidural space. The object of both of these types of injection is to locate an intraspinal tumor or level of compression of the cord from some other cause. The substance used—iodipin—is a poppy-seed oil containing chemically combined iodin to the amount of 0.54 gm. per cubic centimeter. It is said to be nonirritant in the subarachnoid space, and is opaque to the roentgen rays. Sicard recommends 2 c.c. for subarachnoid injection, and 4 c.c. for epidural use. While the article by Sicard and Forestier is illustrated by numerous diagrams representing the oil drops arrested in the neighborhood of obstructions, the short paper by Sargent is accompanied by roentgenograms of three cases in which tumors have been localized by means of the oil, and successfully removed. In Sargent's cases the oil was introduced by cisternal puncture and allowed to settle to the level of the spinal obstruction.

We have for three months experimented with iodipin and with a number of similar oils made up for us by Dr. J. L. Stoddard, chemist at the Massachusetts General Hospital. This experimental work was performed on cats, the oil being injected in 1 c.c. and 1.5 c.c. amounts into the cisterna magna, replacing an equal amount of fluid withdrawn. More recently we have employed

iodipin in two patients, hopeless paraplegics from metastatic spinal disease. These injections were made into the lumbar sac, 2 c.c. and 4 c.c. being used, respectively.

Our experience with the French preparation of iodipin may be briefly summarized as follows:

1. The oil is impervious to roentgen rays, even a small droplet casting a shadow which is not to be confused with normal or pathologic tissue.

2. The oil is disseminated slowly throughout the spinal and cerebral subarachnoid spaces of the cat, under normal conditions.

3. Absorption is extremely slow. One animal, nine weeks after receiving an injection showed most of the oil in the subarachnoid space, much as seen after its introduction.

4. The irritability of the oil was obvious in all of the six animals injected with the French oil. The cats were usually "groggy" for one, two or three days. As an index of irritation of the meninges, it may be noted that in one cat the cell count in the spinal fluid was 4,420, mostly polymorphonuclear leukocytes, on the third day after oil injection. The day after injection, one cat showed a fluid containing 2,700 cells. One animal went into convulsions immediately after an injection and died; at necropsy there was no evidence that the needle had injured the brain.

The irritability of the oil in the two patients was not controlled by reexamination of the spinal fluid, nor were neurologic symptoms significant, because of the completeness of the paralysis in each case. One, however, ran a mildly elevated temperature, otherwise unexplained, for nearly a week after the injection.

5. While we cannot be certain that in our patients the block was localized by the iodipin, as operation was not performed in either case, it is probable that the oil correctly indicated the site of block, in that it was visible nearly up to the level as clinically determined, and did not extend above it.

From our present slight experience, we feel that while iodipin is an agent of probable value in the localization of spinal block, its considerable irritating qualities within the spinal subarachnoid space must be reckoned with; its very slow absorption may also be an important disadvantage. It would seem, therefore, unwise to use this diagnostic procedure as a routine measure; it should be reserved for cases in which clinical and other laboratory methods are insufficient.

DISCUSSION

DR. W. J. MIXTER: Dr. Ayer has said everything that I should want to say except this: I should rather make it a little stronger that I am dissatisfied with this procedure as it stands. I am satisfied that it has a definite application if we can get a nonabsorbable fluid that is opaque, which will rise fairly rapidly instead of disseminating.

DR. P. BAILEY: I am familiar with the French experimenters. I was present when Sicard read the article referred to. We have some iodipin locked up at the Brigham Hospital which we have not used.

THE ANATOMY OF THE INTRACRANIAL SUBARACHNOID SPACES.

DR. HOWARD C. NAFFZIGER of San Francisco, by invitation.

In this paper Dr. Naffziger discussed the subarachnoid spaces on the basis of casts and diagrams with lantern demonstrations.*

*To be published with discussion in the ARCHIVES OF NEUROLOGY AND PSYCHIATRY.